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DIMENSIONS OF AN AGING

POPULATION

**The Impact of Reference Pricing of Cardiovascular Drugs
on Health Care Costs and Health Outcomes: Evidence
from British Columbia – Volume II: Technical Report**

**Paul V. Grootendorst, Lisa R. Dolovich,
Anne M. Holbrook, Adrian R. Levy,
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SEDAP Research Paper No. 71

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**THE IMPACT OF REFERENCE PRICING OF
CARDIOVASCULAR DRUGS ON HEALTH CARE COSTS
AND HEALTH OUTCOMES: EVIDENCE FROM BRITISH
COLUMBIA – VOLUME II: TECHNICAL REPORT**

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Abstract

The Impact of Reference Pricing of Cardiovascular Drugs on Health Care Costs and Health Outcomes: Evidence from British Columbia – Volume II: Technical Report

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Objective: We estimate the effects of Reference Pricing, a drug cost control policy introduced by the BC Ministry of Health Pharmacare program in 1995, on its program expenditures for seniors, out of pocket costs paid by its senior beneficiaries, indicators of beneficiary health status and attendant Ministry of Health expenditures on physicians and hospitals services. **Rationale:** Reference pricing (RP) limits the reimbursement of a group of drugs with similar therapeutic effect but different active ingredients to a fixed "reference price". The setting of the reference price varies by jurisdiction but typically is based on an average of the lowest cost "reference standard" drugs within the group. Critics of RP contend that the partially subsidized and fully subsidized (reference standard) drugs are not therapeutically interchangeable, and therefore patient health will be compromised and use of other non-pharmacologic health services may increase as a result, thus partially or wholly offsetting any potential cost savings from the policy.

Findings: The application of RP to 3 groups of cardiac drugs produced annualized savings to Pharmacare of about \$7.7 million, or 3.6% of the \$213.7 million that Pharmacare spent on drugs for seniors (not including dispensing fees) in 1997. The additional costs for physician consultations were modest, around \$500,000 in the subsample of seniors we studied, from the introduction of the RP plans to March 1998, although the costs could be greater, perhaps up to twice this amount, if we accounted for all seniors exposed to the RP over the same period. We found no effects of RP on mortality, or premature admission to a longterm care facility.

Seniors using the nitrate drugs for angina that were no longer fully subsidized when RP was introduced faced a higher probability in the short run of using medicines to deal with acute exacerbations of angina and in the longer run having bypass surgery or other revascularization procedures. No long run effects of morbidity were observed for the application of RP to two different types of anti-hypertensive medications, although there was a short run increase in the rate of revascularizations among those taking 1 type of anti-hypertensive: the ACE inhibitors. The results of these morbidity models should be seen as tentative, until these results can be replicated using alternative estimation strategies.

Conclusions: The introduction of RP can indeed reduce Ministry of Health drug expenditures. The effects of RP on patient morbidity remain to be fully investigated before definitive policy recommendations can be offered.

Health Transitions Fund Project NA222:

The impact of reference pricing of cardiovascular drugs on health care costs and health outcomes: evidence from British Columbia

Volume II: Technical Report

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Key words: reference pricing, reference based pricing, prescription drugs, utilization, ACE inhibitors, calcium channel blockers, nitrates, pharmaceutical cost control, seniors, copayments, charges, user fees, costs

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1 THE REFERENCE PRICING POLICY

Table 1 presents, for each therapeutic family of cardiac drugs affected by RP, the specific drugs that fall into each category.

1.1 Description of the Reference Pricing policy applied to nitrates.

BC Pharmacare applied RP to nitrate drugs used for chronic prophylactic treatment in 2 stages: Pharmacare beneficiaries whose first prescription for a nitrate was dispensed on or after October 1, 1995 were immediately affected by the policy; Pharmacare beneficiaries who received prescriptions for nitrates before this date were not affected until November 1, 1995. Residents of long term care (LTC) facilities were automatically exempted from RP. As of January 18, 1996, nitrate prescriptions written by pediatricians were also automatically exempted from RP. As a practical matter, the RP exemption status of all Pharmacare beneficiaries is indicated directly on the computerized pharmacy surveillance and claims adjudication network, PharmaNet. Hence the RP exemption for nitrates taken by residents of LTC facilities or patients of pediatricians is applied at the time a reimbursement claim is submitted to Pharmacare.

Hereafter we refer to those drugs whose reimbursement was restricted under the RP policy as 'Restricted'. 'Reference standard' drugs are those drugs whose prices set the level of reimbursement for the Restricted drugs and 'Exempt' drugs are those drugs in the same therapeutic category exempted from the RP policy. The Reference Standard and Exempt drugs are collectively referred to as 'Unrestricted' drugs.

Under RP, reimbursement for a tablet of all dosage forms of isosorbide mononitrate, and pentaerythritol, as well as the sustained-release (SR) forms of both isosorbide dinitrate (ISDN) and nitroglycerin were restricted to the price of a tablet of the lowest cost brand of regular-release ISDN. This limited Pharmacare reimbursement of the Restricted drugs to \$4.60 per 30 day supply, based on a daily dose of 120 mg. Reimbursement decreased to \$4.24 by March 1, 2001 (Table 3). Reimbursement of the transdermal nitroglycerin patch was limited to the price of a 3 inch dose of the nitroglycerin ointment. This limited reimbursement of a 30 day supply of the nitroglycerin patch to \$19.04. The 0.2 and 0.4 mg/hour patches were exempted from RP in January 1996, after the manufacturers voluntarily reduced retail prices, and the 0.6 and 0.8 mg/hour patch strengths were exempted from RP in March 1996. Beginning in September 1998, Pharmacare limited reimbursement of Restricted oral nitrates on the basis of the cost per 30 day supply of ISDN taken at 120 mg/day. The nitrate drugs used for acute treatment, 0.3 and 0.6 mg nitroglycerin tablets, 5 mg ISDN tablets and the nitroglycerin spray, were exempted from RP.

1.2 Description of the Reference Pricing policy applied to Angiotensin Converting Enzyme Inhibitors.

BC Pharmacare applied RP to ACE inhibitors on January 1, 1997, although patients receiving their first refill prescription for a Restricted ACE inhibitor after this date but before April 30, 1997 were eligible for a fully subsidized 2 week supply. Pharmacists were able to contact Pharmacare for this authorization. Before the policy was introduced, Pharmacare identified all beneficiaries who had previously taken medication for asthma or diabetes and identified them as

being exempt from RP on the PharmaNet. As this was a one-time exemption, patients who became eligible for Pharmacare benefits after January 1, 1997 and used drugs for asthma or diabetes were reliant on their physicians to apply for Special Authority exemption on their behalf.

Unlike nitrates, for which Pharmacare reimbursement was initially limited to a fixed price per unit of the medication, reimbursement of the ACE inhibitors and CCBs was always limited to a fixed cost per 30 day supply. Hence, individuals taking sufficiently low doses of Restricted drugs such that the total monthly ingredient cost was under the reimbursement limit continued to receive reimbursement as per usual Pharmacare policy. The RP policy initially limited remuneration for several ACE inhibitors – benazepril, cilazapril, enalapril maleate, enalapril maleate + hydrochlorothiazide, lisinopril, lisinopril + hydrochlorothiazide and fosinopril – to \$27.00 for a 30 day supply. Reimbursement decreased to \$26.37 by March 1, 2001 (Table 2). Captopril, quinapril, and ramipril are the reference standard medications and are reimbursed as per normal Pharmacare policy.

1.3 Description of the Reference Pricing policy applied to Dihydropyridine Calcium Channel Blockers

BC Pharmacare applied RP to the dihydropyridine calcium channel blockers on January 1, 1997, although patients filling their first refill prescription for a Restricted CCB after this date but before April 30, 1997 were eligible for a fully subsidized 2 week supply. At the time the policy was introduced, Pharmacare identified all patients who had previously taken medication for asthma or diabetes and identified them as being exempt from RP in the PharmaNet. As this was a one-time exemption, patients who became eligible for Pharmacare benefits after January 1, 1997 and used drugs for asthma or diabetes were reliant on their physicians to apply for Special Authority exemption on their behalf. CCB prescriptions written by a nephrologist, cardiologist, internist or other physician who requested and received Pharmacare approval were flagged in the PharmaNet as being exempted from RP reimbursement restrictions.

The RP policy initially limited remuneration for several dihydropyridine CCBs – amlodipine, nifedipine, and both regular- and sustained release nifedipine – to \$31.00 for a 30 day supply. Reimbursement gradually decreased to \$30.48 by March 1, 2001 (Table 3). Felodipine is the reference standard medication and is reimbursed as per normal Pharmacare policy; two other CCBs – verapamil and diltiazem – are exempt from the policy.¹ Sustained release versions of verapamil and diltiazem are, however, subject to a variant of the Low Cost Alternative policy. The standard LCA policy restricts remuneration to the lowest priced brand of the drugs with identical active ingredient, dosage form and strength; the variant of LCA applied to the sustained release versions of verapamil and diltiazem restricts remuneration of these drugs to the lowest available prices of identical dosage strengths of the regular release versions. Residents of long term care facilities (Pharmacare Plan B) are automatically eligible for full coverage of generic versions of sustained release diltiazem and verapamil.

¹ Felodipine, verapamil and diltiazem constitute the Unrestricted CCBs.

Table 1 Varieties of patient exemption from reference pricing of cardiac drugs in British Columbia

Special authority (SA) exemptions are provided to patients whose physicians have successfully petitioned Pharmacare. Only those applications that provide a valid reason for exemption are approved; Pharmacare has, however, provided physicians with a list of acceptable reasons. SA exemptions provided to ACE inhibitors and CCB users were valid indefinitely. SA exemptions provided to nitrates users before January 21, 1997 were valid for just 1 year; SA exemptions provided thereafter never expired.

Therapeutic trial exemptions from RP of ACE inhibitors and CCBs are provided for a period of 6 months to particularly frail patients who likely require several trials of anti-hypertensives before adequate blood pressure control is reached. Application for this exemption requires the physician send a case description to Pharmacare.

Automatic exemptions require no action on the part of the patient or prescriber to initiate. These are given to Pharmacare beneficiaries who have used drugs for asthma or diabetes in some time period *before* the introduction of RP (ACE inhibitors and CCBs only). These exemptions are valid indefinitely. Other automatic exemptions are provided to prescriptions dispensed to residents of longterm care facilities (nitrates only), or dispensed by specific specialists approved by Pharmacare (CCBs and nitrates only).

One-time exemption – individuals filling their first refill prescription for a Restricted drug after the introduction of RP are given a two-week supply reimbursed as before the RP policy (ACE inhibitors and CCB only). Pharmacists could apply directly for this. Nitrate users filling a refill prescription were eligible for a one-time fully reimbursed 2 week supply starting in February 1996 – over 3 months after the introduction of the policy.

De facto exemptions – Pharmacare limited reimbursement of ACE inhibitors and CCBs to the cost of a 30 day supply on the reference standard drugs in each category. Individuals taking sufficiently low doses of restricted ACE inhibitor and CCB drugs such that the total drug ingredient cost per 30 days was below the reference price were therefore not affected by RP. Until August 31, 1998, Pharmacare reimbursement of nitrates was limited to a fixed price per unit (tablet or patch). After this time, reimbursement was limited to a price per 30 day supply.

Table 2 Cardiac drug groups targeted by the Reference Pricing policy in British Columbia

Therapeutic Category	Implementation Date (Announcement date)	Restricted Drugs	Unrestricted Drugs Reference Standard	Exempt	Automatic Exemptions	Special Authority Exemptions ¹
Nitrates Used for stable angina	October 1, 1995 if starting nitrate therapy on or after 95-10-1. November 1, 1995 if already using nitrates on 95-10-1. ² (August 25, 1995)	Isosorbide mononitrate both regular and sustained release (SR), Nitroglycerin (NTG) SR tablets, Pentaerythritol both regular and SR, Isosorbide Dinitrate SR, NTG Patch ³	Isosorbide Dinitrate ⁴ , and NTG Ointment ⁵	0.3 and 0.6 mg NTG tablets, 5 mg isosorbide dinitrate tablets, and NTG spray	Resident of a long-term care facility; patients of pediatricians (after Jan. 18, 1996)	No special exemptions.
ACE inhibitors Used for hypertension, congestive heart failure and diabetic nephropathy	January 1, 1997 ⁶ . (October, 1996)	Benazepril, Cilazapril, Enalapril Maleate, Enalapril Maleate + Hydrochlorothiazide, Fosinopril, Lisinopril + Hydrochlorothiazide, and Lisinopril.	Captopril, Quinapril, and Ramipril	None	Patients with concomitant use of medication for asthma or diabetes prior to January 1, 1997	Patients with congestive heart failure, chronic renal disease, asthma or diabetes. ⁷
Calcium channel blockers Used for hypertension and stable angina	January 1, 1997 ⁶ . (October, 1996)	Amlodipine, Nicardipine, Nifedipine SR, and Nifedipine.	Felodipine	Verapamil, Diltiazem ⁸	Same as for ACE inhibitors, plus patients dispensed drugs by a nephrologist, cardiologist or cardiology internist.	Patients with coronary artery disease, asthma, diabetes, arrhythmias. ⁷

Notes

1. All patients: experiencing treatment failure or an adverse reaction on the reference standard product; or experience a drug/drug interaction with the reference standard product; or who are frail and elderly and undergoing complex multi-drug therapy; or who are cognitively impaired for which changing medications may represent a threat to compliance are eligible for Special Authority. This column indicates any additional indications for Special Authority unique to the therapeutic category. Special Authority exemptions for nitrates were initially given for a period of 1 year, after which the physician had to re-apply. Effective January 21,

1997, nitrate Special Authority exemptions were provided indefinitely. Special Authority exemptions for ACE inhibitors and calcium channel blockers were given indefinitely.

2. As of February 19, 1996, pharmacists could contact Pharmacare to request a one-time 2-week Special Authority exemption for patients who required a refill of their nitrate medication and who were unaware of the policy change and needed some time to contact their physician. This temporary exemption policy lasted approximately three months.
3. The 0.2 and 0.4 mg/hour transdermal nitroglycerin patches were exempted from RP in late January 1996 after the manufacturers reduced prices. The 0.6 and 0.8 mg/hour strengths continued to be referenced until late March 1996. The 0.3 mg patch was made available to Pharmacare beneficiaries only after this time and was never restricted.
4. The reference standard drug for the oral nitrates.
5. The reference standard drug for the transdermal nitrates.
6. Between January 1 – April 30, 1997, patients filling their first refill prescription for a Restricted ACE inhibitor or CCB were eligible for a 2 week extension. Pharmacists are able to contact Pharmacare for this authorization.
7. Special Authority exemptions require the physician to specify the Restricted drug for which full reimbursement is requested; exemptions are given for a period of 1 year. Physicians have the option of applying for a ‘Therapeutic Trial’ for frail patients taking Restricted ACE inhibitors or calcium channel blockers. This will fully reimburse any Restricted drug for a period of 6 months.
8. Long acting versions of verapamil and diltiazem are subject to a variant of the Low Cost Alternative policy. This policy restricts remuneration of the long acting versions of these drugs to the prices of identical dosage strengths of the shorter acting versions. Residents of long term care facilities (Pharmacare plan B) are automatically eligible for full coverage of generic versions of long acting diltiazem and verapamil.

Table 3 Pharmacare reimbursement per 30 day supply of Restricted drugs, by effective date and therapeutic category

Therapeutic Category	October 1, 1995	November 1, 1995	January 1, 1997	before July 1, 1999	July 1, 1999	November 1, 1999	March 1, 2001
H2 Antagonists	\$11.00			\$10.61	\$10.51	\$10.52	\$10.52
NSAIDs				\$12.98	\$13.01	\$12.95	\$12.95
Nitrates	\$4.60	\$4.62		\$4.24	\$4.24	\$4.24	\$4.24
ACE inhibitor Inhibitors			\$27.00	\$26.36	\$26.36	\$26.37	\$26.37
Dihydropyridine CCBs			\$31.00	\$30.50	\$30.36	\$30.30	\$30.48

2 RESEARCH QUESTIONS

Our objective is to evaluate whether the reference pricing (RP) policy, as applied to the nitrates, angiotensin-converting-enzyme (ACE) inhibitors and dihydropyridine calcium channel blockers (CCBs), has reduced Pharmacare drug expenditures on its senior (65+ years) beneficiaries without adversely affecting their health status (cardiovascular disease related mortality and morbidity) or increasing expenditures on hospital and physicians' services reimbursed by the BC Ministry of Health. Specific indicators of morbidity include hospital admissions for cardiovascular disease and associated length of stay, revascularization, prescriptions of sublingual nitroglycerin, physician hospital and emergency room consults, physician ambulatory consults, and surgical and diagnostic physician services related to cardiovascular disease. We also examined the distributive effects of the policy. How much did seniors pay for the partially subsidized 'Restricted' drugs? To what extent did individuals' income affect access to Restricted drugs?

2.1 Seniors vs other Pharmacare beneficiaries

Even though the RP policy was applied to most Pharmacare beneficiary groups, including welfare recipients (Plan C) and households with large drug costs relative to income (Plan E), we decided to focus on Pharmacare senior beneficiaries (Plan A) for two reasons. First, seniors have the highest rates of per capita consumption of the cardiovascular medications targeted by the RP policies, have above average rates of comorbidities and hence any adverse events from RP would likely be detected in this group. Second, historical prescription claims data is not comprehensive for individuals whose Pharmacare eligibility status can vary over time (Plan C), or for individuals who face deductibles (Plan E). Data on prescription drug use for BC residents 65 years and older are relatively comprehensive because, except for reasons of death or out of province migration, their beneficiary status does not change over time.

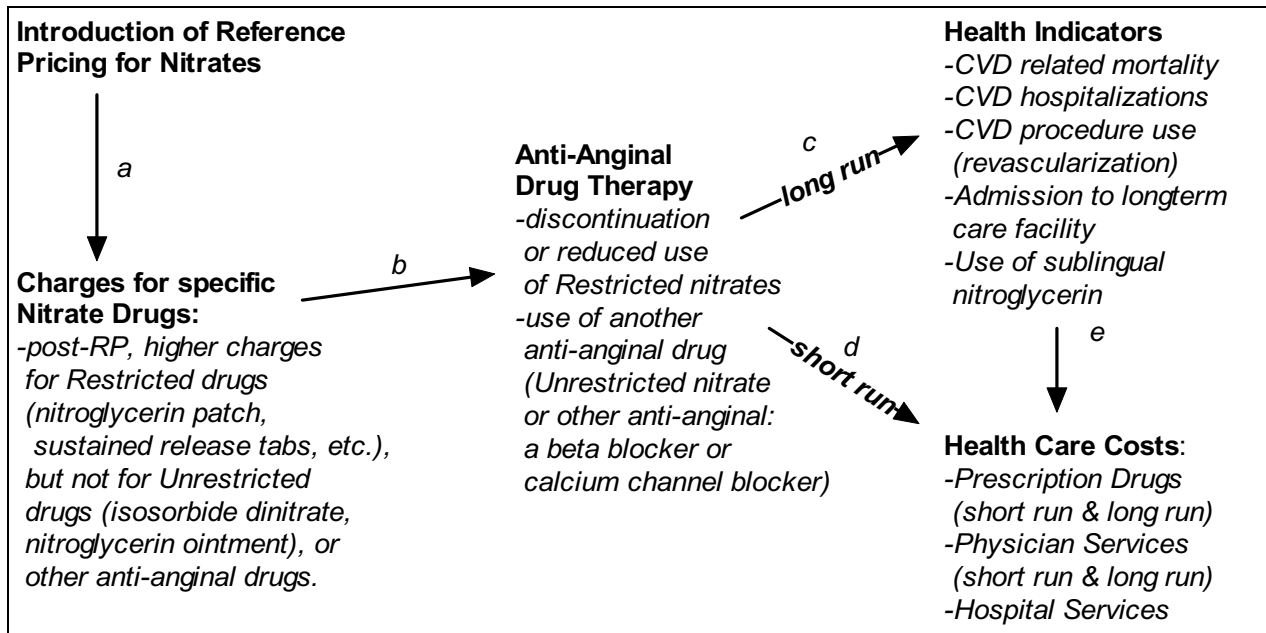
2.2 Conceptual framework

We focus on the effects of the RP policy on those seniors who, prior to the introduction of RP, were taking drugs whose reimbursement was eventually restricted under RP. These subjects are to be distinguished from the senior Pharmacare beneficiaries who initiated use of nitrates, ACE inhibitors or CCBs *after* the introduction of the policy.² As we discussed below, the effects of RP are likely to be different in the two groups of subjects.

Figure 1 outlines the potential effects of RP of nitrates on health care costs and health outcomes in a cohort of seniors who were taking nitrates before the introduction of the policy. The sequence of events associated with the introduction of RP of the ACE inhibitor and CCB drugs on health care cost and health outcomes should be similar, although the types of outcomes affected by the application of RP to these drugs might differ.

² These individuals are not examined in this study because of the difficulties of estimating their outcomes had they not been exposed to the RP policy.

Figure 1 Schematic of the potential effects of reference pricing of nitrates on nitrate users at the time of policy introduction



The effects of nitrates RP on charges for nitrates and other anti-anginal drugs (process a)

In the model considered here, the primary source of any changes in health care costs or health outcomes associated with RP occurs through changes in the amount that subjects are required to pay (hereafter ‘charges’) for Restricted nitrate drugs. In general, the Pharmacare subsidy for nitrates, and hence charges for these drugs, will vary both across time (pre-post RP) within subjects and across subjects (post-RP). Prior to the nitrates RP policy, Pharmacare subsidized, to varying degrees, the ingredient cost of nitrate drugs listed on the Pharmacare formulary.³ With the introduction of RP of nitrates, for some but not all subjects, Pharmacare limited reimbursement of the ingredient cost of Restricted drugs to the unit price of the reference standard drug. The Unrestricted nitrates (i.e., the reference standard and exempted nitrates) remained subsidized as per normal Pharmacare policy for all beneficiaries.

Post RP, there is no additional charge for Restricted drugs for those who receive an exemption from the policy. Non-exempted subjects face an additional charge equal to the difference

³ Seniors were responsible for the dispensing fee, up to a \$200 annual maximum and in some cases were responsible for some of the drug ingredient cost. Under the ‘Low Cost Alternative’ (generic substitution) program, Pharmacare limited reimbursement of different brands of interchangeable drugs – drugs with identical active ingredient, dosage form and strength – to an average of the lowest priced brands. Starting February 1999, reimbursement was limited to the lowest price brand. Both of these policies have been in effect since April 1994, 18 months prior to the introduction of nitrates RP. In addition, the ‘Maximum Price Policy’ introduced in June 1995, sets the maximum Pharmacare drug reimbursement equal to manufacturers’ list prices for direct purchases or 9% (7% after January 1, 1997) above list price for pharmacy purchases from a drug wholesaler.

between the retail price of the Restricted drug and the (fixed) Pharmacare subsidy. Hence the larger the retail price of the Restricted drug, the bigger the patient's charge.

The effects of changes in charges for nitrates on their anti-anginal drug therapy (process b)

Nitrate drugs are typically prescribed for the management of angina. This condition can also be managed, however, with calcium channel blockers (CCBs) or beta blockers. Subjects and/or their physicians (our data do not identify how drug use decisions are arrived at) are modeled as deciding how much of each anti-anginal drug to consume, depending on the relative charges of all anti-anginal drugs. An individual with neither private insurance nor a RP exemption will find Unrestricted nitrates or other anti-anginal drugs less expensive than Restricted nitrates. Whether the price change is a binding constraint, however, depends on the nitrate drug that was used when the policy was introduced. Individuals taking an Unrestricted nitrate could have taken a Restricted nitrate when it was free of charge, but chose not to. Hence they would likely not use a Restricted nitrate when its charge increased, unless changes in their condition after the introduction of RP required it. On the other hand, individuals initially taking a Restricted nitrate now face an additional charge and are more likely to partially reduce use of the Restricted nitrate, completely discontinue use, or begin using an Unrestricted nitrate or another fully subsidized anti-anginal drug (such as a beta blocker or CCB – at least Unrestricted CCBs and Restricted CCBs taken prior to the introduction of RP for these drugs in January 1997).

In addition to the variables identified above (type of nitrate taken when nitrates RP was introduced, private insurance coverage, RP exemption status), the probability of a change in anti-anginal drug therapy following RP depends on subjects' income or wealth – subjects can pay out of pocket to obtain a Restricted nitrate. Moreover, some physicians might be inclined to switch all of their patients taking Restricted drugs to Unrestricted drugs, irrespective of their patients' insurance status or income.

The effects of changes in anti-anginal drug therapy on health status (process c)

Changes in anti-anginal drug therapy might affect subjects' health for several reasons:

1. Seniors might reduce the amount of the Restricted drug they consume below the point where the drug has full therapeutic effect.
2. Patient health could be compromised if Restricted drugs are more effective, have better side effect profiles and/or induce better patient compliance than Unrestricted drugs. On the other hand, some patients could be switched to a drug which works better for them. The quantitative importance of differences between these drugs is uncertain, however, because there are few head-to-head comparisons between these drugs reported in the medical literature. The clinical trial evidence which is available indicates that there are no 'clinically important' differences between them; a review of the evidence on the therapeutic differences between Restricted cardiac drugs is provided in the accompanying Volume III (ACE inhibitors and CCBs), and Holbrook *et al* (1997) [1] (nitrates). The effectiveness of the drugs as they are used in practice, however, which will be influenced by factors such as drug compliance, is less well known.

3. Switching between Restricted and Unrestricted drugs requires that the patient adjust to a new therapy. Therapeutic switches *per se* could produce adverse physiologic effects and could also be detrimental if the patient perceives the change in therapies to be harmful and if this belief translates into lower physiological or mental health [2]. There is little published evidence on the health effects of switching.
4. While it is possible that RP itself could adversely affect patient health, it is also possible that RP could lead to the discovery of health problems that existed prior to the introduction of the policy. Some of those using Restricted drugs pre-RP will consult their physicians post-RP to discuss their treatment options (i.e., switch drugs, change the dose, apply for a special authority exemption) and possibly meet again to monitor progress on a new drug. These additional physician interactions could reveal underlying health problems that otherwise would not have been discovered until later. Hence an association between RP and morbidity (as measured by the use of health services) might not necessarily indicate that RP ‘causes’ morbidity.

The change in health following a change in drug therapy will likely vary by subject; the health change might depend, for example, on contraindications, co-medications, co-morbidities, and age. It is also likely that the effect of a change in drug therapy on health is not instantaneous, but rather operates with a lag.

The direct effects of changes in subjects’ drug therapy on their health care costs (process *d*)

Changes in subjects’ drug therapy could potentially directly affect health care costs in both the short run and longer run.

Effects on short run prescription drug costs. Given that the prices of Restricted drugs can vary substantially, limiting reimbursement to the cost of the lowest priced drug is guaranteed to reduce Pharmacare’s drug expenditures if subjects previously taking a Restricted drug either pay out of pocket the difference between the retail price and the Pharmacare subsidy, or reduce use of their Restricted drug, or switch to an Unrestricted drug. But, as was noted earlier, there might be factors that limit savings: a large number of patients might be exempted from RP, in which case Pharmacare will continue to subsidize their Restricted drugs at pre-RP levels. Patients taking sufficiently low doses of the Restricted drugs, such that their monthly drug ingredient cost is below the reference price, are also unaffected by the policy. In addition, physicians might substitute relatively expensive drugs that are used for the same indication but are not directly targeted by the RP policy, thereby offsetting the drug cost savings [3;4]. Finally, economic theory suggests that setting reimbursement rates on the basis of the prices of a set of reference standard drugs might encourage the manufacturers of these drugs to raise prices [5;6]. On the other hand, manufacturers of Restricted drugs might lower their prices to gain additional market share – and these price cuts might provide savings to other drug insurers and payers. Hence the net effect of RP on the prices charged by manufacturers is ambiguous.

Effects on physicians’ services costs. As was mentioned above, RP might increase expenditures on physicians’ services in the short run, as those using Restricted drugs pre-RP consult with their physicians to decide on their post-RP therapy.

The effects of changes in subjects' health indicators on their health care costs (process *e*)

Changes in subjects' morbidity will likely affect health care costs. For example, those patients whose angina was worse because of a switch to a less effective drug might use more acute 'rescue' therapy (the first line of which is sublingual nitroglycerin) resulting in additional drug expenditures. Patients who develop uncontrolled hypertension as a result of a switch in CCB or ACE inhibitor medication may be at higher risk for a stroke or myocardial infarction, thereby incurring additional hospital and physician-related services. Similarly, discontinuation of ACE inhibitors may lead to more congestive heart failure events.

Note that the effects of RP on health care costs are unclear if the disruption of drug therapy associated with RP reduces longevity; in this case, the lifetime health care costs of those affected by RP could decrease. We take up this issue in the Methods section below.

Distributional consequences of RP

We also assess some of the distributional effects of RP: To what extent does seniors' ability to pay affect their use of the higher priced Restricted drugs? To obtain a Restricted drug after the introduction of RP, Pharmacare beneficiaries can either pay the additional charge or receive an exemption, in which case Pharmacare pays the additional charge. Using patient-level data, we modeled how senior's income status (an indicator of low income) affected both the probability of exemption from RP, and, in the subsample of seniors who were not exempted, the amount paid for Restricted drugs. If RP adversely affects patient health status, then assessing the extent to which income improves access to Restricted drugs provides evidence about the equity of this policy.

2.3 Defining exposure to Reference Pricing

Fundamental to our RP evaluation strategy was the definition of exposure to RP. Exposure to RP can be defined in several ways, each with its own advantages and limitations.

Changes in post-RP drug use. Some analysts define exposure to RP using an intermediary outcome of RP, that is post-RP *changes* in drug use. In particular, analysts sometimes use *switches* from a restricted to an unrestricted drug, or to a drug outside the therapeutic group which can nonetheless be substituted for the Restricted drug (e.g. beta blockers can be substituted for nitrates for the management of stable angina). The purported advantage of comparing the outcomes of those who switch drugs against those who do not is that it can inform the health consequences of changes in patients' drug regimens. This advantage is offset by several limitations.

First, one needs to identify the *contribution* of RP to switching probabilities: some likely would have switched anyway⁴ and hence it would be incorrect to attribute the consequences of all switches to RP. Presumably, in the absence of RP, therapeutic changes would be made in an

⁴ For example, some individuals initiating anti-anginal drug therapy require trials of several drugs to determine which drug works best; hence some may have switched between Restricted and Unrestricted nitrates and other anti-anginal drugs in any event.

attempt to improve patient care. If such switches are health improving, but RP-induced switches are not, then average post-switch health of *all* switchers would be over-estimated. On the other hand, if rates of switching prior to the introduction of RP were low, then this may not make a practical difference.

Second, comparing switchers to non-switchers introduces selection bias: beneficiaries can continue to receive normal Pharmacare reimbursement for their Restricted drugs post-RP (and not switch) if they receive an RP exemption. But exemptions are ostensibly targeted at those who are less able to tolerate a switch (see Table 2). Hence non-switchers might be less healthy than switchers.⁵ In addition, those who die for reasons unrelated to RP before they have a chance to switch medications will be counted as non-switchers and this will complicate interpretation of the effects of RP on both mortality and morbidity among the survivors.

The third limitation of defining RP exposure on the basis of post-RP drug use is that one needs to enumerate, measure and model all of the changes in drug use that might affect outcomes. Defining exposure on the basis of drug switching status, for example, will be complicated if those who do not switch instead pay out of pocket to remain on a Restricted drug. Those who pay, in an attempt to save money, might reduce their consumption below the point where the drug provides full therapeutic effect. Here the comparison of switchers vs. non-switchers will be affected by confounding: some non-switchers face higher charges and this might affect their drug consumption. And attempts to define subjects' exposure on the basis of their post-RP level of drug use might introduce yet another form of sample selection bias that would tend to attenuate any adverse effects of RP: Individuals with unusually low drug use, who are otherwise healthy, would be assigned as low drug users, while those with unusually high drug use, who are otherwise less healthy, would be assigned as high drug users. Over time, the average health of the low drug users would increase, while the average health of the high drug users would decrease.

Comparison of those who face higher charges for restricted drugs against those who do not.

The chain of events between the introduction of RP and subsequent health care and health status outcomes begins with the increase in patient charges for Restricted drugs (Figure 1). Higher charges might lead to switching from and/or reductions in the use of Restricted drugs, which in turn could affect subjects' health and expenditures on health services. Instead of defining exposure on the basis of changes to drug use following increased patient charges, one could define exposure on the basis of exposure to the higher charge itself. Two groups of subjects did not face additional charges under RP and are potential comparators to those that did: those who used Unrestricted drugs pre-policy, and those who used Restricted drugs pre-policy who were continuously eligible for exemption from RP.⁶ The Unrestricted drug users could have used a Restricted drug when it was fully reimbursed but chose not to, hence the copayment increase is likely non-binding, assuming that the propensity of those on Unrestricted drugs to switch to

⁵ This will not necessarily be true in all cases. Pharmacare adjudicates special authority exemption requests by ensuring that a valid reason has been transcribed. But Pharmacare has provided physicians with the list of acceptable reasons for a special authority exemption and there is no risk of audit. Moreover, anecdotal reports suggest that physicians differ in their willingness to incur the (uncompensated) time and effort costs to apply for exemption, and also in the 'illness severity' thresholds used to determine which patients are eligible for exemption.

⁶ Those with private insurance which provides full or partial subsidies for Restricted drugs would not face the full extent of the price increase.

Restricted drugs is low. We present some confirmatory evidence below. Those who receive RP exemptions continuously post-RP, by definition, continue to receive normal Pharmacare reimbursement for their Restricted drugs and hence do not face higher charges. Identification of subjects who do and do not face increases in charges for Restricted drugs captures all of the potential effects of the policy and hence obviates the need to enumerate and measure *a priori* the potentially deleterious post-RP changes in drug use, but adoption of this method comes at the expense of being uninformative as to how the attendant changes in drug use affect outcomes.

Identification of subjects who were not exposed to RP by virtue of their continuous use of Unrestricted drugs pre-RP is relatively straightforward, and is described below. Identification of those who received continuous exemptions, on the other hand, is less straightforward. Some exemptions are time-limited, such as prescriptions written by exempt specialists (Table 1). In such cases, one needs to determine the effective period of exemption on the basis of an estimate of the days supply of the exempted prescription, and repeat this for all exempted prescriptions to ensure that there were no lengthy gaps during which the subject was exposed to the higher charges for Restricted drugs.

Use of these comparator groups might also introduce some sample selection bias, and this is likely to be worse for the exemptees: For most subjects, exemption status is identified by the receipt of exemptions for Restricted drugs dispensed post-RP. But some or all of the post-RP drug use records are missing for those who died, migrated out-of-province, or were hospitalized. Those who died before being dispensed any Restricted drugs post-RP, or were hospitalized for the duration of their post-RP follow up period would be categorized as not having received an exemption and hence would be ‘exposed’ to the additional charges for Restricted drugs. Below, we present some evidence on the extent of sample selection bias using exemptees as comparators. Identification of those who used Unrestricted drugs pre-RP, on the other hand, does not use post-RP drug use and is not subject to this problem, but is subject to a special form of selection bias: Individuals are often prescribed drugs on the basis of the nature and/or severity of their health conditions, hence the pre-RP morbidity of those using Restricted drugs might differ from those using Unrestricted drugs. Naive comparisons of the post-RP outcomes of the two groups will be confounded by pre-existing differences in their morbidity.⁷

The problems with the use of post-RP drug use to define RP exposure favor comparing subjects according to their use of Restricted or Unrestricted drugs pre-RP. But identifying the impact of RP using this approach changes the interpretation of the estimates – they now indicate the mean difference in outcomes of those who were *potentially* exposed to RP, irrespective of their post-RP changes in drug use, to those who were not exposed. Included in the group of the potentially exposed are those with insurance for the additional charges for Restricted drugs and those who received special authority exemptions throughout their post-RP follow up period who, by definition, would not have been affected by the policy. The inclusion of such subjects in the exposed group would hence dilute the average treatment effect, with dilution being greater, the greater the number of (pre-RP) Restricted drug users insured or exempted.⁸ We nevertheless

⁷ This selection bias is sometimes referred to as ‘assignment bias’ in the epidemiological literature.

⁸ The effect of RP on those potentially exposed to the policy will also be affected by the prevalence of drug insurance coverage for the differential charges for Restricted drugs (which is not observable in the data) – the greater the prevalence of insurance coverage, the lower the impact of RP.

believe that this approach has its merits. Because it avoids the biases introduced by selecting individuals on their drug use after the introduction of RP, the ‘average effect’ parameters are likely better estimated. Second, the proportion of subjects who are exempted is an inherent feature of the RP policy, as it is determined by the strictness of exemption criteria and enforcement mechanisms; all of these policy design features will influence the average effect parameters. Third, the average effect estimates are key inputs into cost benefit analyses of RP. Finally, defining exposure on the basis of pre-RP Restricted vs. Unrestricted drug use will provide more informative estimates of the effect of RP on the additional physician visits made by patients to discuss treatment options. Those taking Unrestricted drugs pre-RP would not need to consult with their physicians for this purpose, while those taking Restricted drugs pre-RP might. In future work, we will remove from the group of pre-RP Restricted drug users those who subsequently were continuously exempted from RP to better estimate the effects of the policy on the outcomes of those who were not exempted.

2.4 Effects of Reference Pricing on prevalent vs incident cohorts

We focus on the effects of the RP policy on those senior Pharmacare beneficiaries who, prior to the introduction of RP, were taking drugs whose reimbursement was eventually restricted under RP. We refer to these individuals as the ‘prevalent’ cohort. The effects of RP on this group will likely differ from the effects of RP on the group we refer to as to ‘incident’ cohort – those senior Pharmacare beneficiaries who initiated use of nitrates, ACE inhibitors or CCBs, *after* the introduction of the policy. Both cohorts were potentially affected by RP, but in different ways: in the prevalent cohort, RP increased the charges of medications already being used, whereas those in the incident cohort made their initial choice of medication in light of the higher charges for Restricted drugs. Consider the individuals in each of the cohorts who neither received exemption from RP nor paid out of pocket to use a Restricted drug. Such individuals in the prevalent cohort switched their medications, whereas those in incident cohort did not switch – they simply started therapy on an Unrestricted drug or substitute. To the extent that Restricted drugs are superior to Unrestricted drugs and substitutes, individuals in both incident and prevalent cohorts who do not use Restricted as a result of RP are harmed by the policy. But those in prevalent cohort are at greater risk from any adverse events due to drug switching. Hence our estimates of the effect of RP on the prevalent cohort likely provide an upper bound on the adverse health events associated with the effect of the RP policy on the prevalent cohort.

The group of seniors that we examine in this study faced a sudden change in the reimbursement of the higher priced drugs that were targeted by RP. Successive generations of senior Pharmacare beneficiaries may or may not face the same surprise. This depends on the age that individuals commence therapy for the drugs targeted by RP, and their level of anticipation of the policy. Individuals who are already eligible for senior (age 65+ years) Pharmacare benefits when initiating therapy, will make their initial choice of medication with knowledge of the higher charges for Restricted drugs. Those who initiate drug therapy while under age 65, and ineligible for Pharmacare benefits, might very well anticipate their upcoming eligibility for Pharmacare benefits, and elect to start on a Unrestricted drug. Alternatively, those who anticipate the RP restrictions might purchase supplemental drug insurance prior to reaching age 65, so that they face no additional charges irrespective of their choice of medication.

3 METHODS

3.1 Data

The British Columbia Ministry of Health (BC MoH) is the payer of first resort for most medical services, hospitalizations, longterm care facility stays and prescription drugs for senior (65+ years) residents, and collects patient-level health service use data for purposes of provider/hospital remuneration. It also collects vital statistics (mortality) and links this to health services use data. The BC MoH provided (anonymized) patient-level, linked administrative health services billing and vital statistics data covering the period January 1993 to November 1998 for those Pharmacare senior beneficiaries (65+ years) who had at least 1 CCB, Nitrate, or Beta Blocker prescription dispensed to them over the same period of time, January 1993 to November 1998. The same health services data was provided for the period January 1993 to March 1998 for those who were dispensed at least 1 ACE inhibitor over the period January 1993 to March 1998. For each subject, we have a record of every prescription drug dispensed (for which Pharmacare paid at least a portion of the cost), every medical service delivered by fee-for-service remunerated physicians, every hospitalization in a publicly funded BC acute care hospital, every admission in a publicly funded BC long-term care facility, and a record of date and ICD-9 coded cause of death. In addition, we had basic demographic information – patient birthdate and sex, limited information on patient income, and the Forward Sortation Area (the first 3 digits of the postal code) of the residence of the subject. At no time could individual patients be identified in the data.

In addition to the patient-level claims data, we had access to monthly Pharmacare claims data (over the period January 1993 – May 1999) on drug-specific prescriptions dispensed, quantities dispensed, Pharmacare and patient-reimbursed drug ingredient cost and Pharmacare-reimbursed drug dispensing fees aggregated over all senior Pharmacare beneficiaries. Because these data capture Pharmacare claims for all senior beneficiaries, they are better able to address the effects of RP on drug expenditures than the subsample of seniors that we used to identify the effects of RP on mortality and morbidity.

3.2 Construction of variables

3.2.1 *Pharmacare and patient prescription drug expenditures*

We used monthly expenditures data that were aggregated across all Pharmacare's senior beneficiaries. For each different nitrate, ACE inhibitor and CCB, and for each month over the period January 1993 – May 1999, we assembled data on total Pharmacare and patient-paid drug ingredient expenditures (but not dispensing fees), per 100,000 seniors [7], total 'defined daily doses' dispensed per 100,000 seniors, and average Pharmacare reimbursement per defined daily dose. These variables were also calculated at the drug group level (nitrates, ACE inhibitors and CCBs) and for the drug groups that are potential substitutes (beta blockers, alpha blockers, diuretics, central acting medicines and vasodilators, and ACE-2 receptor blockers). The number of defined daily doses dispensed is defined as $\sum_j qty_j \times mg_j / ddd_j$; the number of units (tablets, etc.) of the j th dosage strength of the drug dispensed (qty_j) times its dosage strength, measured in

milligrams per unit (mg_j) divided by ddd_j – the defined daily dose of the drug⁹ based on the January 1998 World Health Organization definitions [8], all summed over the j different dosage strengths of the same drug.

The aggregate data permit examination of the trends in expenditures of substitute drugs before and after RP – this might identify whether RP increased costs on drugs not directly targeted. To better identify this, in future research we will use patient-specific prescribing data on those who were using Restricted drugs pre-policy to estimate switching rates to substitute drugs post-policy.

3.2.2 *Mortality*

While cause-of-death specific mortality information is available in our data, clinical measures of cardiovascular disease (CVD) related morbidity are not. Instead, morbidity was measured by the use of selected health services associated with CVD, such as ambulatory physician consultations, hospital admissions (both emergent and non-emergent) for myocardial infarction, congestive heart failure, stroke, and renal conditions, and hospital-based procedures (cardiac catheterization, angioplasty, bypass surgery), and time to admission to a long term care facility after the introduction of RP (which signals that more intensive medical supervision is required than that allowed by home care). In the event that RP increased the use of health services, we estimate the cost of the additional health services used.

We had access to two sources of mortality data: Vital Statistics data on both date and cause of death over the period January 1992 to December 1997, inclusive; and date of death information for subjects who passed away in hospital from January 1992 until November 1998 (nitrates users) and March 1998 (ACE inhibitor and CCB users). Even though the in-hospital death data span a longer period of time than do the Vital Statistics data, these data are less comprehensive, as death outside of hospital is not captured. We therefore focused on the Vital Statistics data. These data will provide a 12-month follow up period after the RP of ACE inhibitors and CCBs, and a 26-month follow up period after the RP of nitrates. We distinguished between death that could have been caused by RP – diseases of the circulatory system (3 digit level ICD-9 codes 390 – 459), diabetes (250), and renal disease (584-588) – and death due to all other reasons. Evidence that RP increases the likelihood of death from other causes casts suspicion on the specification of our statistical models.

3.2.3 *Health indicators based on prescription drug records*

Subjects whose angina was worsened by the RP policy might use more acute ‘rescue’ therapy, the first line of which is (short-acting) sublingual nitroglycerin. These drugs, which were exempted from the nitrates RP policy, consist of 0.3 and 0.6 mg nitroglycerin tablets, 5 mg ISDN tablets and the nitroglycerin spray. We assembled data on the number of Pharmacare-reimbursed prescriptions for sublingual nitroglycerin by subject and month.

⁹ The DDD represents the assumed average maintenance dose per day for a drug when used for its main indication in adults, and is assigned to each chemical substance (defined as a fifth level Anatomical Therapeutic Chemical class).

3.2.4 Health indicators based on hospitalization records

Every acute care hospitalization in a publicly funded hospital in BC generates a discharge abstract which contains information on admission and discharge dates, the *Primary Discharge Diagnosis* (PDD) – the health condition which was primarily responsible for the patients hospital stay – as well as the procedures performed while in hospital. Using these data, we identified subjects who were hospitalized for cardiovascular disease related conditions, tracked their hospital length of stay for such conditions and identified any surgical procedures related to their health condition.

The PDD is coded using the International Classification of Disease, 9th revision (ICD-9). We identified those subjects who were admitted to acute care hospitals¹⁰ and whose PDD fell within the following categories:

<i>Health Condition</i>	<i>ICD-9 Coded Primary Discharge Diagnoses*</i>
Ischemic Disease	410-414, 440, 429.2
Hypertension	401-405
Congestive Heart Failure	428
Stroke	431-436
Dysrhythmias	427
Peripheral Vascular Disease	441-444
Cardiovascular Disease Symptoms	785
Hypotension	458
Diabetes	250
Renal Disease	584-588

* For each 3-digit level ICD-9 code listed, we included all of the 4 and 5 digit level sub-codes.

In addition to the frequency of acute care hospital admissions, for each PDD category we also determined subjects' length of stay (LOS) in days in acute care hospitals. To do so, we calculated $LOS_t = D_t - A_t + 1$, where A_t is the admission date of the t^{th} hospitalization, and D_t is the associated discharge date. Two adjustments were made to LOS. First, all LOS values over 90 days are indicative of an acute care bed being used for a chronic care patient, typically while waiting for a transfer. We truncated LOS at 90 days, assuming that a maximum of 90 days could have been spent receiving acute care. Second, LOS calculations were adjusted to avoid double counting when the subject was hospitalized while not having been discharged from the previous hospitalization. This happens when inpatients are temporarily transferred to another hospital for specialized care and are subsequently transferred back. Formally, this occurs when hospitalizations are *encompassed* within other hospitalizations (Figure 2):

$$A_t > A_{t-1} \text{ and } D_t < D_{t-1}, \text{ or} \\ A_t \geq A_{t-1} \text{ and } D_t < D_{t-1}, \text{ or}$$

¹⁰ We removed about 4% of all hospitalizations in our data that were not for the provision of acute care. These included *Level of Care* values of “discharge planning/GEAR units”, “Extended Care/CBD Units”, “Intermediate Care”, “Long-Term Care patients in Acute Care Beds”, “Rehabilitation” and “Day Care Surgery”.

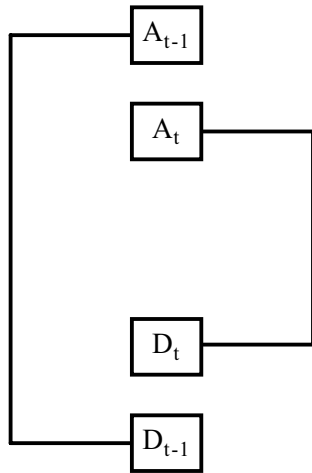
$$A_t > A_{t-1} \text{ and } D_t \leq D_{t-1}, \text{ or}$$

$$A_t = A_{t-1} \text{ and } D_t = D_{t-1}.$$

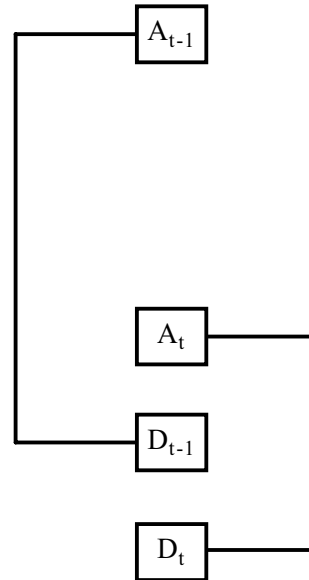
In such cases, we dropped the encompassed observation, and used the PDD of the initial hospitalization. Another potential source of double counting occurs for *partly encompassed* hospitalizations, which occur when $A_t < D_{t-1}$ and $D_t > D_{t-1}$. In these cases, we set $A_t = D_{t-1}$.

Figure 2 Types of encompassed hospitalizations

Encompassed hospitalizations.



Partly encompassed hospitalizations.



For the purposes of calculating the frequency of hospital admissions, encompassed hospitalizations were dropped, but partly encompassed observations were not. We then found the number of hospital admissions and hospital LOS by health condition, subject and month. The LOS data were adjusted so that the days in hospital were assigned to the months of the stay. For example an individual admitted January 30 and who spent 20 days in hospital would be recorded as having spent 2 days in hospital in January and 18 days in hospital in February.

Once hospitalized, individuals might receive surgical treatment of acute myocardial infarction, occluded coronary arteries, stable or unstable angina. Such treatment consists of two procedures: angiography and revascularization.¹¹ Angiography and revascularization (both coronary artery bypass grafting and percutaneous transluminal coronary angioplasty) performed within hospitals

¹¹ Angiography is a diagnostic technique that provides images of how blood flow to the heart may be compromised. Revascularization comprises one of two techniques, coronary artery bypass grafting (CABG) or percutaneous transluminal coronary angioplasty (PTCA). CABG circumvents an occlusion of the coronary arteries by bypassing it using a section of an artery or vein taken from elsewhere in the body. PTCA consists of threading a catheter across a partially occluded artery then inflating a balloon in order to improve blood flow through the artery. Revascularization is never done without prior angiography, because one must determine the sites of occlusions in order to revascularize.

were identified in the hospital discharge records using the following Canadian Classification of Diagnostic, Therapeutic and Surgical Procedures (CCDTSP) codes:

<i>Procedure</i>	<i>CCDTSP Codes</i>
Angiography	48.92 – 48.98 and 49.95 – 49.97
Coronary artery bypass grafting (CABG)	48.11 – 48.19
Percutaneous transluminal coronary angioplasty (PTCA)	48.02 – 48.05 and 48.09

3.2.5 *Health indicators based on physician service records*

We categorized physician fee codes into 8 groups:

1. Ambulatory (non-hospital) physician consultations
2. Emergency and hospital consultations
3. Cardiovascular disease-related surgical procedures
4. Cardiovascular disease-related diagnostic procedures
5. Renal surgical & diagnostic procedures
6. Renal dialysis
7. All other services
8. Non-service related fees

We selected variables 2-4 as health indicators, as they were potentially affected by disruptions in the use of the cardiac drugs targeted by RP. The number of ambulatory physician consultations (variable 1) was used to assess the administrative costs associated with the implementation of the RP policy. It is possible however that ambulatory physician visits could also be due to higher morbidity, but this is difficult to identify separately. Variables 5-6 were measured to control for morbidity differences between subjects that existed prior to the introduction of RP in the statistical health outcomes models. We included all other services (variable 7) primarily for the purposes of determining whether RP had spill over effects on the cost of physician services not directly associated with RP. The description of the fee codes in each of these categories is provided in Appendix C.

Unlike the hospital-based health indicators, which capture activity for inpatients only, physician services data captures activity in both inpatient and ambulatory care settings. One drawback of these data is that they do not capture the provision of services by physicians who are not remunerated on a fee for service basis. Given that many emergency room physicians receive salaries, we will not identify those subjects who entered a hospital emergency room, was seen by a salaried physician and then released. On the other hand, if the severity of the condition did not warrant hospitalization then we are censoring less severe cases only.

3.2.6 *Health care costs*

The perspective of the BC Ministry of Health was adopted for the purposes of identifying the costs of the RP policy, a decision made solely on the basis of data availability. As a result, the

time and other costs incurred by physicians who fill out Special Authority exemption forms, pharmacists who are often faced with explaining the terms of the RP policy to patients, and patients who incur the time costs of additional physician visits, while possibly non-trivial, are not considered here. Moreover, we do not consider the costs incurred by Pharmacare in implementing the RP policy, nor the cost of Pharmacare personnel who adjudicate Special Authority exemption requests. Finally, we do not quantify the personal health care costs, or forgone income of patients whose health might be adversely affected by the policy.

3.2.6.1 Prescription drug costs

We measured Pharmacare-paid drug ingredient cost and dispensing fees for sublingual nitroglycerin, as well as for the drug groups that are potentially substitutable for the cardiac drugs targeted by RP.

3.2.6.2 Physician services costs

For each of the groups of physician fee codes defined earlier, we found total BC Ministry of Health expenditures per subject and month. Expenditures were defined as gross physician payments (as defined by the BC Medical Services Commission fee schedule) less any adjustments that were made to ensure that physician billings did not exceed personal or global expenditure caps. Payments do not include Northern Isolation Allowance or interest payments for delayed payments.

3.2.6.3 Hospital costs

Unlike physicians' services and prescription drugs, the BC Ministry of Health does not reimburse hospitals on a fee-for-service basis. Instead, the Ministry of Health sets hospital budgets annually. However, for each hospital discharge there is information that classifies subjects into groups with similar levels of health care resource use and supplementary data exist to estimate the resource utilization (ultimately measured in dollars) for each group. The Case Mix Groups (CMG) system, developed by the Canadian Institute for Health Information, groups individuals discharged from hospital by levels of expected resource use on the basis of their age, sex, primary discharge diagnoses, (i.e. the health condition most responsible for the patients hospital stay), secondary diagnoses (i.e., co-morbid conditions present upon hospital admission), procedures performed during the hospitalization, the patients discharge status – (1) dead, (2) normal, (3) transfer, (4) signed out against medical advice, and an indicator of whether the patient had an unusually long hospital length of stay.

Each CMG has an associated Resource Intensity Weight (RIW), which is a measure of the hospital's resources consumed by a particular CMG relative to some numeraire service. The RIWs used in this study are based primarily on U.S. (Maryland), not Canadian hospital case costing data.¹² As such the relative resource use of different CMGs might not be representative

¹² Resource Intensity Weights developed using case costs specific to Canada (primary Ontario) has recently been made available. (See <http://www.cihi.ca/direct/13apr2000.shtml>.) We were unable to use these data, however, because these RIWs apply to the Case Mix Group definitions that were operational only after the end of our sample window (March 1998).

for BC hospitals. On the other hand, our primary goal is to assess *differences* in hospitalizations and surgical/diagnostic procedure use between Exposed and comparator groups and if there are no differences, then costing is not necessary. Moreover, we have access to physician-related costs (at least those remunerated directly by the Ministry of Health) for inpatient procedures (these costs are not included in the RIW data), so accurate costing information for at least a portion of the hospital-based services is available.

To convert RIWs to dollars, we used estimates of the BC-specific average cost per RIW (i.e., cost per weighted case [9]). This was constructed by summing the weights assigned to all cases treated in a sample of hospitals in the province, and dividing this number into the hospitals' total inpatient expenditure. The resulting cost per RIW, in 1997 dollars, for British Columbia is \$2,722.

3.2.7 *Exemption from Reference Pricing and out of pocket payment*

The patient-level Pharmacare claims data contained two pieces of information to ascertain exemption status: a RP exemption identifier (created by Pharmacare) and the amount of patient copayment. We first assessed the validity of the exemption identifier on each Restricted nitrate/ACE inhibitor/CCB (including the patch during the periods in which its various dosage strengths were restricted) dispensed to all subjects from the RP implementation dates to the end of the sample windows. The RP exemption identifier was useless for identifying nitrates RP exemptions, as this variable was introduced into the claims data in October 1996, well after the introduction of nitrates RP. The validity of this variable was suspect for claims after October 1996 as well. We cross-tabulated the exemption indicator with an indicator of whether or not the subject paid out of pocket for the ingredient cost of the Restricted drug. If the indicator were valid, one would expect prescriptions free of charge to be flagged as having received an exemption. In many cases, this was not the case. As an example, 44% of the 20,003 prescriptions of nitroglycerin 2.6 mg sustained release tablets that were free of charge to the patient were not identified as having received an exemption.

Given that the validity of the SA exemption indicator was suspect, we created our own RP exemption indicator using the patient copayment data on prescriptions for Restricted drugs dispensed after RP. We determined patient-paid ingredient cost charges per unit of each Restricted drug prescribed, and if nothing was paid, the prescription was treated as RP-exempt. (Given the potential for rounding error, per unit patient payments under \$0.01 were defined as being zero.) Prescriptions for which charges were paid could still have received an exemption if the charges were due to two other reimbursement restriction policies already in place before RP. These include the Low Cost Alternative (LCA) policy of restricting payment of drugs within a multi-sourced drug category (i.e. drugs with identical active ingredient, dosage form and strength) to the lowest price (typically "generic") drug in the group. Unless an exemption is specifically provided for a brandname drug, the patient is responsible for the price difference between the brandname and generic drug cost. In addition, the Maximum Price Policy (MPP) sets the maximum Pharmacare drug reimbursement equal to manufacturers' list prices for direct purchases or 9% (7% after January 1, 1997) above list price for pharmacy purchases from a drug wholesaler. Pharmacies are known to pass on their drug expenses in excess of the maximum allowable price to Pharmacare beneficiaries.

We identified RP-exempted prescriptions by invoking the assumption that patient payments for non-exempted prescriptions of Restricted drugs were larger than the patient payments due to MPP and LCA. To identify typical charges due to MPP, for each single-sourced drug category, we used the 95th percentile of per unit charges in the 4-month period preceding the introduction of RP (July – October, 1995 for RP of nitrates; September – December, 1996 for RP of ACE inhibitors and CCBs). Because RP had not yet been introduced over this period, and because there were no generics in the drug categories examined, any charges had to have been due to MPP. We assumed that these charges applied throughout the post-RP period. Subjects paying less than the typical MPP amount for single-sourced drugs were assumed to have received a RP exemption. To identify typical charges due to LCA, for each multi-sourced drug category and month, we computed the median Pharmacare full reimbursement for brandname and generic drugs respectively and defined the LCA ‘brandname upgrade’ charge as the difference between the two. (‘Full’ reimbursement refers to the amount Pharmacare paid for prescriptions in which there were no patient charges. We focused on these prescriptions to isolate LCA charges from RP charges.) Charges for multi-sourced drugs under the greater of this amount and the MPP charges were assumed to have received a RP exemption.

To assess the distributional effects of RP, we modeled the effect of income on the probability that patients were continuously exempted from RP and on the amount paid for Restricted drugs in the subsample of those who did not receive exemption. Patient exemption was determined on a per-prescription basis using the algorithm described above. Some patients could have been exempted for some prescriptions and could have paid for others. Those identified as having received continuous exemptions, included those who received exemption for all the Restricted drugs taken after the introduction of RP. Individuals who received exemptions for all of their Restricted drugs post-RP and received their first exemption prior to initiating therapy on an Unrestricted drug or substitute¹³ were identified as being continuously exempted from RP and were used as comparators for Exposed subjects. In addition to these subjects, we included those subjects who paid for up to 2 Restricted drugs immediately after the introduction of RP and then received exemptions for the remainder, subject to the restriction that they did not switch therapy from a Restricted to an Unrestricted drug or substitute prior to the receipt of their first exemption. This rule included seniors who, initially unaware of the RP policy when refilling prescriptions for restricted nitrates and unable to contact their physicians to obtain an exemption, elected to pay out of pocket, but avoided paying for subsequent prescriptions of Restricted nitrates by receiving an exemption. In addition, we included subjects who received RP exemptions for restricted nitrates, (again prior to the initiation of therapy on an Unrestricted drug or substitute) but who elected to pay for up to 2 prescriptions when their nitrates RP exemptions expired in late 1996 - early 1997, and then once again received exemptions. (Up until January 21, 1997, exemptions for Restricted nitrates were time-limited.) Those who received RP exemptions for ACE inhibitor and CCBs and then temporarily paid for such drugs were not categorized as having received RP exemptions continuously because exemptions for these drugs were provided indefinitely. Patient payment for Restricted drugs was measured over the period

¹³ The requirement that the first RP exemption be received prior to initiation on an Unrestricted drug was made to exclude those subjects who initiated a trial on a Unrestricted drug and eventually returned to a Restricted drug. The initiation of therapy was defined by at least 5 consecutive weeks of non use of the drug followed by 3 or more weeks of continuous use of the drug. Continuous drug use was defined according to the algorithm already used to identify pre-RP drug use.

ending 1 year after the introduction of RP (November 1996 for nitrates and January 1998 for ACE inhibitors and CCBs).¹⁴

3.2.8 *Switching from a Restricted to an Unrestricted drug or substitute*

Another important intermediary outcome of the policy is the rate of switching from a Restricted to an Unrestricted drug or substitute. To identify switching, we first identified the weeks that each subject was continuously using each Restricted drug, Unrestricted drug and each potential substitute using the algorithm described below¹⁵. Next, we identified the week(s), if any, that each subject terminated therapy on a Restricted drug and initiated therapy on an Unrestricted drug or substitute. Therapy termination was defined as 5 or more consecutive weeks of drug use followed by 3 or more consecutive weeks of non-use. The first week of non-use was identified as the therapy termination week. Therapy initiation was defined as 5 or more consecutive weeks of no drug use followed by 3 or more consecutive weeks of use. The first week of drug use was identified as the therapy initiation week. A switch was said to have occurred if therapy on an Unrestricted or substitute¹⁶ was initiated during the 15 weeks before or after the discontinuation of therapy on a Restricted drug. We allowed the initiation of Unrestricted drug therapy to precede the discontinuation in the event that a subject received a prescription for a Unrestricted or substitute drug during the same week that they filled their final prescription for a Restricted drug. We allowed up to 15 weeks overlap because the maximum days supply allowed by Pharmacare is 100 days, or 14.29 weeks. We allowed the initiation of Unrestricted drug therapy to follow the discontinuation by up to 15 weeks in the event that the subject needed the time to consult with his or her physician to get the prescription changed.

3.2.9 *Patient Income*

Limited subject-specific income information is available from the MOH Medical Service Plan (MSP) data. MSP charges premiums¹⁷ for health care but offers subsidies based on income, as well as age of applicant, age of spouse if married, and the disability status of each household member (see Table 4). The subsidy amounts decrease monotonically with income, so it is possible to infer income ranges on the basis of the subsidy level, as long as one knows the other characteristics affecting eligibility for subsidy.

¹⁴ Our definition of the subjects who were continuously exempted from RP, while a useful first start, might include those who in fact were not continuously exempted. Some might have had extended periods of time when no drugs were used at all. In future work, we will attempt to ensure that continuous exemptees did not have disruptions in their use of Restricted drugs.

¹⁵ The NTG Patch was treated as both a Restricted and Unrestricted drug, depending on when use occurred. The drug was treated as Restricted from October 1, 1995 (1 month prior to RP of nitrates) in anticipation of the policy up until the time that the reimbursement of the drug was no longer restricted by RP: the end of the 3rd week of January 1996 (for the 0.2 and 0.4 mg/hr patch) and the end of the 13th week of 1996 (for the 0.3, 0.6 and 0.8 mg/hr patch).

¹⁶ Substitutes for nitrates for the management of stable angina include CCBs and beta blockers. Substitutes for ACE inhibitors (for the management of hypertension, congestive heart failure or renal nephropathy) are a CCB, diuretic, alpha blocker, beta-blocker, ACE-2 receptor blocker, central acting drug, or vasodilator. Substitutes for CCBs (for the management of stable angina or hypertension) include a: maintenance nitrate, beta-blocker, ACE inhibitor, diuretic, alpha blocker, ACE-2 receptor blocker, central acting drug, or vasodilator. [0]

¹⁷ These premiums are effectively taxes because they are not based on expected health care use. Moreover, individuals cannot be denied access to health care if premiums are not paid.

Table 4 BC Medical Services Plan premium subsidies by level of adjusted net income: 1994-1998

Adjusted Net Income*	MSP Premium Subsidy	MSP Code
\$0 - \$11,000	100%	A, D, H
\$11,000.01 - \$13,000	80%	B
\$13,000.01 - \$15,000	60%	F
\$15,000.01 - \$17,000	40%	G
\$17,000.01 - \$19,000	20%	E
\$19,000.01+	0%	C

* Adjusted net income is defined as net income (as defined on the income tax return) less \$3,000 for the applicant, less \$3,000 if the applicant is 65+ years, less \$3,000 if the applicant's spouse is 65+ years, less \$3,000 for each disabled household member, less 50% of child care expenses.

Given that we do not observe all the characteristics required to measure senior's household income intervals, in particular age of spouse if married and household members' disability status, we opted to identify subjects who received a MSP premium subsidy over the 13-month period ending the month RP was implemented. This binary indicator of low income is prone to less measurement error than are the multiple indicators of income ranges. But the binary indicator of low income is subject to another source of error. Preliminary results from research comparing tax file income data with premium assistance coverage has demonstrated that, of those single BC residents (of all ages) who do not receive any premium assistance, 21% are in fact eligible for some. On the other hand, almost all (98%) of those who do receive premium assistance are in fact eligible [10;11].

3.2.10 Identification of Exposed and Non-exposed groups

For the purposes of estimating the effect of RP on morbidity, physician and hospital related health care costs and mortality, we focus on Pharmacare senior beneficiaries who were continuous users of Unrestricted and Restricted drugs prior to the implementation of the nitrates RP policy in November, 1995 and the ACE/CCB RP policy in January 1997. The RP policies were announced several weeks in advance of policy implementation (late August to early September, 1995 for the nitrates; October, 1996 for the ACE/CCB drugs), and to ensure that we selected our sample of both exposed and comparator groups on the basis of drug use that was unaffected by the awareness of the upcoming RP policy, we identified those subjects who were continuous drug users before widespread anticipatory Restricted to Unrestricted drug switching was likely – September 23, 1995 (nitrates) and November 3, 1996 (ACE inhibitors/CCBs).

To identify periods of continuous medications use, we extracted the dispensing history for each subject and for each Restricted and Unrestricted maintenance nitrate, ACE inhibitor and CCB. Using the patient and drug-specific data on each prescription dispensal date (d_t), the subsequent prescription dispensal date (d_{t+1}), the number of units dispensed (q_t), and the potency (or strength) of the drug in mgs/unit (mg_t), we calculated the average number of mgs dispensed per

day between successive prescription dispensing dates as: $mpd_t = (q_t \times mg_t) / (d_{t+1} - d_t + 1)$.¹⁸ If mpd_t fell below a threshold value (defined as the smallest available drug potency per unit reimbursed by Pharmacare), the dispensing date of the prescription in question signaled the interruption of a spell of continuous therapy.¹⁹ To allow for the possibility that mpd_t was temporarily low owing to the earlier dispensation of an unusually large quantity of drugs (in which case the subject could still have been consuming this earlier prescription), we computed a revised mg per day estimate averaged over the current and previous prescription: $mpdl_t = (q_{t-1} \times mg_{t-1} + q_t \times mg_t) / (d_{t+1} - d_{t-1} + 1)$, where the 't-1' subscript refers to the previous prescription. If $mpdl_t$ exceeded the threshold, then no interruption in therapy was deemed to have occurred. We obtained estimates of mg per day averaged over the previous 2 prescriptions, as well as the previous 3 prescriptions and repeated the procedure.

The starting date of each spell of continuous therapy was set as the dispensing date of the first in the sequence of uninterrupted prescriptions. The ending date of the spell was the date of the prescription in which average daily mgs used fell below the threshold, plus an estimate of the days supply for that prescription. The days supply estimate was the number of mgs dispensed ($q_t \times mg_t$) divided by the maximum of the median mpd for the spell in question and the defined daily dose [8] for that drug. We then identified the weeks during which the subject was in the midst of a spell of continuous drug therapy. To be considered a continuous nitrate drug user pre-RP, the subject had to have taken a maintenance nitrate drug at least 19 of the 20 weeks during the period ending September 22, 1995. Continuous users of ACE inhibitor and CCB drugs were defined as those taking such a drug at least 19 of the 20 weeks during the period ending November 2, 1996

Continuous users of nitrates, ACE inhibitors and CCBs were classified as (1) those that used only Restricted drugs pre-RP, (2) those that used only Unrestricted drugs pre-RP or (3) those that used both Restricted and Unrestricted drugs pre-RP. We excluded the latter group from subsequent analysis because we could not identify their primary nitrate medication. Continuous users of ACE inhibitor and CCB drugs were themselves divided into 3 groups: (A) those using only ACE inhibitors pre-RP, (B) those using only CCBs pre-RP and (C) those using both types of drugs pre-RP. Individuals in the latter group were potentially affected by the application of RP to 2 or their medications at the same time, and could have endured the most deleterious impact of the policy. We elected to focus on groups (A) and (B) and left examination of group (C) subjects for future research, however, due to time constraints.

3.3 Identifying the effect of exposure to Reference Pricing on outcomes

Fundamental to our research design is a means of disentangling the effects of RP on outcomes from the effects of other factors. These other factors include: (1) time-invariant differences in the characteristics of those who we define as potentially exposed (i.e., Restricted drug users pre-RP) and those unexposed (i.e., Unrestricted drug users pre-RP); and (2) factors that change over

¹⁸ The potency of the nitroglycerin patch is measured as a rate of nitroglycerin (in mgs) released per hour. Given that the patch is normally worn for a 12-hour duration, the effective mgs delivered per patch is the hourly rate times 12.

¹⁹ To find the smallest drug potency unit for the nitroglycerin ointment, which is dispensed from a tube, we used the 10th percentile of the empirical distribution of $mpdt$ which was 0.5"/day. The median was 1.25"/day.

time. The methods available to identify the effects of RP depend on the nature of both the outcome variable being modeled and the data used.

3.3.1 *Drug expenditures*

We assessed the effects of RP on Pharmacare-reimbursed drug expenditures on nitrates, ACE inhibitors and CCBs taken using monthly claims data aggregated across all seniors. Estimates of the effect of RP on drug costs using these data are derived from a comparison of drug expenditures pre-post RP and are subject to bias due to the effects of ‘confounding’ variables – variables correlated with both the introduction of RP and with expenditures. Confounding occurs if pre-RP trends in expenditures, extrapolated into the post-RP period, do not reflect what would have happened in the absence of RP. One potential confounder are changes in the rates of prescribing of the drugs targeted by RP, due to factors such as changes in prescribing guidelines, or the availability of substitute medicines.

To deal with the possibility that such confounders biased our estimates, we estimated the effects of RP under different assumptions about the presence of confounders. The first assumption was that there was no such confounding: any changes in the total volume of drugs dispensed within each of the 3 drug categories targeted by RP (nitrates, ACE inhibitors and CCBs), were due to RP. If for example, prescribing volumes of all nitrates dropped after the introduction of RP, this was entirely due to RP. Hence RP reduced Pharmacare expenditures by reducing both the reimbursement price per nitrate and the volume of nitrates dispensed. The effect of RP was estimated using the standard pre-post RP comparison of expenditures.

The second assumption was the converse of the first: any changes in the volume of drugs dispensed before and after RP would have happened regardless of RP. Hence any reductions in Pharmacare expenditures due to RP are a sole result of reductions in Pharmacare reimbursement prices. To operationalize this assumption, we decomposed average monthly expenditures for each drug group targeted by RP into the product of prices (the average Pharmacare reimbursement per defined daily dose of the drug dispensed per month) and quantities (the number of defined daily doses of the drug dispensed per month). Under this assumption, prices are potentially affected by RP, but quantities are independent of RP. The effect of RP on expenditures is then the *change* in reimbursement prices attributable to RP times the volume on drugs dispensed. The results from this approach were compared to the results from modeling expenditures directly to see if results were robust. Throughout our analysis we maintained the assumption that our estimates of the effect of RP on Pharmacare reimbursement prices were not subject to confounding. This assumption is perhaps more plausible than a similar assumption regarding prescribing volumes. For example, we could identify no other Pharmacare policies during our sample period that could have affected reimbursement prices. On the other hand, changes in the mix of drugs within each of the drug groups targeted by RP could have affected the average reimbursement price. In future work, we will use prescribing data from another province such as Ontario to help infer counterfactual outcomes.

Estimation of the effect of the RP policy on expenditures on the CCB drugs is confounded with the concurrent application of a variant of the LCA policy to the Exempt CCB drugs, whereby the sustained release versions of diltiazem and verapamil were reimbursed at the same price as the

same effective dosage strength of the regular release versions of the same drugs. We therefore considered the effects of both the CCBs RP and the reimbursement restrictions on the SR versions of verapamil/diltiazem on use and expenditures on all the CCB drugs.

Estimation of the effect of RP on patient-paid drug ingredient expenditures for Restricted drugs could have been a straightforward matter of adding up cumulative patient expenditures for these drugs post-RP. Some of these expenditures, however, were the result of 2 other Pharmacare policies, introduced before RP, which required patient copayments: the LCA and MPP policies. To estimate the effect of RP on patient expenditures, we therefore extrapolated trends in patient spending starting with the introduction of the LCA policy in April 1994 into the RP period. We did this for each of the individual drug groups targeted by the policy and for all of the drug groups combined.

3.3.2 *Mortality and admission to longterm care facilities*

Comparing the post-RP time to death or admission to a longterm care facility among the potentially exposed vs. the comparators necessarily requires between-subject comparisons, but these two groups will likely differ in their pre-RP morbidity.²⁰ We controlled for these differences by covariate adjustment using statistical time-to-event (survival) models.²¹ To ensure that the conclusions are robust, we also compared the (unadjusted) 1 year survival of those who used Restricted and Unrestricted drugs pre-RP with the (unadjusted) 1 year survival times of those who were using Restricted vs. Unrestricted drugs 1 year *prior* to the onset of RP. The difference in survival of the former group is potentially affected by both RP and a baseline morbidity difference, while the difference in survival of the latter group is potentially affected by a baseline morbidity difference only. Hence the difference in the two estimates should identify the effect of RP on survival, assuming that the baseline morbidity differences and their effect on morbidity remain stable over the course of the year.

²⁰ For example, there is evidence that users of the nitroglycerin patch, a Restricted drug which was commonly prescribed at the time of the introduction of RP, had higher levels of morbidity relative to those using Unrestricted nitrates. One reason is that the patch manufacturers sold the patch to hospitals at heavily discounted prices in an attempt to promote the use of the nitroglycerin patch among outpatients. Hence some exposed subjects were initially prescribed the patch while in hospital.

²¹ These covariates include age at introduction of RP, sex (female vs male and unknown), low income status, interaction between sex and age, interaction between income status and sex, an indicator of the drug taken continuously before RP (e.g. the specific nitrate drug used in the subsample of nitrate drug users), and the use of health services in the 12 month period before the introduction of RP, by service type. These included the number of prescriptions of sublingual nitroglycerin, gastric suppressing drugs targeted by RP, other gastric suppressing drugs, anti-inflammatory drugs targeted by RP, all other anti-inflammatory drugs, and the number of prescriptions for drugs for the disease management, by disease type: diabetes, vascular disease, hypercholesterolemia, epilepsy, rheumatic disease, cancer, Parkinson's disease, glaucoma, cystic fibrosis, thyroid disorders, gout, Crohn's disease, respiratory disorders, depression, psychoses, bipolar disorder, anxiety, and all other prescriptions; the days supply of ACE inhibitors, CCBs, nitrates, diuretics, alpha blockers, beta blockers, vasodilators and central acting medicines, and ACE2 receptor blockers; the number of physicians' services delivered by service type, including non-hospital consultations, emergency and hospital based visits, CVD related surgical procedures, CVD related diagnostic procedures, renal surgical and diagnostic procedures, renal dialysis, and all other service types; hospital length of stay for CVD related conditions, hospital length of stay for all other conditions; number of cardiac revascularization procedures (PTCA, and CABG) performed in hospital, and the number of other procedures performed in hospital; and finally an indicator of pre-RP longterm care admission.

If those exposed to RP face higher mortality rates than those not exposed, then the estimates of the effect of RP on morbidity and health care costs on those who survive are potentially biased. Suppose that the probability of survival depends on the level of morbidity²², with sicker subjects more likely to die. If RP makes individuals sicker, and the sickest individuals are more likely to die, then the average health of the surviving subjects exposed to RP will increase over time. On the other hand, the survivors will be at risk for other diseases, hence the impact on attrition on their health (and health care costs) is ambiguous. Whether or not the estimation technique used needs to be adjusted to control for this form of selection bias depends on the results of the comparison of differential mortality between those exposed and not-exposed to RP. If required, several methods are available to adjust for this bias [12-14].

3.3.3 *Morbidity and costs of physician and hospital services*

We had longitudinal data on morbidity indicators and the cost of physicians' and hospital-based health services. Longitudinal data consist of observations on the same subjects over multiple time periods, and our estimation methods exploit the structure of these data. Specifically, the inclusion of subject-specific indicator variables (commonly called 'fixed effects') in the statistical models of each outcome variable was used to control for subject-specific time-invariant factors, observed or otherwise, that affect outcomes. Furthermore, to control for time-varying confounders²³, we compare the pre-post RP change in outcomes of the exposed to the pre-post RP change in outcomes of those not exposed to the policy. If the effects of time-varying confounders on the outcomes of the Exposed and non-exposed are similar, and if outcomes are the sum of the separate effects due to RP, patient fixed effects and time-varying confounders, then subtracting the pre-post RP change in outcomes of the non-exposed (which are affected by confounders only, not RP) from the pre-post RP change in outcomes of the Exposed (which are affected by both confounders and RP) will isolate the effect of RP on outcomes. This is called the "difference-in-differences" (DD) design [15;16]. To test the adequacy of the assumption that, in the absence of RP the outcomes of the exposed and unexposed have similar time trends, we estimated the difference in pre-RP rates of change of the outcomes over time between the exposed and non-exposed. If the DD design is consistent with the data, the trends should be similar. The test was conducted by estimating a fixed effect linear regression model of the outcome variable as a linear additive function of a linear time trend and the interaction between the linear time trend and an indicator of those subjects exposed to RP. The models were estimated using monthly data starting with data 16 months prior to the introduction of RP and ending ending 3 months before RP introduction. A rejection of the hypothesis that the coefficient on the interaction variable is zero raises questions about the adequacy of the DD design.

If the use of the DD model is inappropriate, then an alternative method of identifying the effects of RP on outcomes is to examine the pre-post RP differences in outcomes of those exposed to the policy. Employing this method will not control for the effects of time-varying confounders (such

²² In which case attrition from the data set is said to be 'informative' or 'non-ignorable'.

²³ Time varying confounders include seasonal effects, changes in clinical practice, and the effects of changes in provider remuneration by the Ministry of Health. One notable change was the elimination in the fall of 1996 of several commonly used fee codes for ambulatory physician consultations. This resulted in a marked drop in consultations.

as aging, increases in disease severity over time, the effects of attrition bias), but this method is still useful if one can sign the bias. Suppose that, even in the absence of RP, subjects' health deteriorates over time. Then the pre-post RP difference in health will be biased towards showing that RP is harmful. Yet if RP is found to be harmless despite this bias, there is some evidence that it is in fact harmless.

3.3.4 Probability of exemption and amount paid out of pocket

Using patient-level data, we modeled how seniors' income status (an indicator of low income) affected both the probability of continuous exemption from RP, and, in the subsample of seniors who were not exempted, the probability of payment and the amount paid for Restricted drugs in the year following the introduction of RP. We used data on those who were using Restricted drugs prior to RP, and who survived at least 1 year after the introduction of RP. The latter restriction was imposed to avoid confounding due to death – if lower income seniors die sooner than do higher income seniors, then they might also spend less on Restricted drugs.

To identify the effect of income status on exemption and payment, we modelled these outcomes as being linear functions of the low income indicator and a variety of potential confounding variables.²⁴ There is some evidence that, among the entire population of residents of BC, the low income indicator was measured with error. If this is equally true for our sample of seniors, then our estimates of the effect of income on both the probability of exemption from RP and the amount paid out of pocket in the subsample of those who were not exempted from RP will be downwards biased. In this case, the absolute value of the estimates represents the lower bound on the effect of income on the outcomes studied.

Special attention needs to be paid to the interpretation of how income affects the amount paid for Restricted drugs. Income affects ability to pay directly, but also indirectly through its effect on the prior acquisition of supplementary drug insurance. While we cannot disentangle the separate effects of income and insurance coverage on the amount paid for Restricted drugs, we can infer the net effect of income on these variables.

²⁴ These covariates were patient age at the introduction of RP, sex, indicators of the Restricted drug used prior to RP, as well as the number of defined daily doses of the drug used in the year prior to the introduction of RP. We also included use of the following health services in the year prior to the introduction of RP: hospital length of stay for CVD related conditions, hospital length of stay for all other conditions; number of cardiac revascularization procedures (PTCA, and CABG) performed in hospital, and the number of other procedures performed in hospital; an indicator of pre-RP longterm care admission; the number of physicians' services delivered by service type, including non-hospital consultations, emergency and hospital based visits, CVD related surgical procedures, CVD related diagnostic procedures, renal surgical and diagnostic procedures, renal dialysis, and all other service types; the number of prescriptions dispensed for: sublingual nitroglycerin (nitrates models only), diabetes, and respiratory conditions. The latter two variables were included because special authority exemptions from the RP as applied to the ACE inhibitors and CCBs were given to subjects with diabetes and asthma.

3.4 Statistical Methods

3.4.1 *Drug costs*

For each cardiac drug group targeted by RP, we estimated models of both monthly Pharmacare expenditures, and average Pharmacare reimbursement per defined daily dose per month. These variables were modeled as linear additive functions of a constant, a linear time trend, and 2 RP indicator variables, one shortrun and one longrun. The shortrun indicator was included to account for any transitory effects on drug costs. For example, there is evidence that Pharmacare beneficiaries stockpiled drugs before the introduction of a dispensing fee copayment in April 1987 – these drug stockpiles were consumed several months after the copayment increased. Stockpiling of the higher priced Restricted drugs could also occur after the announcement of RP. Also, subjects refilling prescriptions were given 2-week temporary exemptions from RP; this lasted for several months after the introduction of RP (Table 1). In addition, the 0.2 and 0.4 mg/hour NTG patch was removed from RP in the third week of January 1996. The shortrun indicator was equal to 1 starting with the RP announcement month (September 1995 for nitrates, October 1996 for ACE inhibitors and CCBs) up to 3 months post policy (January 1996 for nitrates and March 1997 for ACE inhibitors and CCBs). The longrun indicator was equal to 1 starting with the announcement of RP.

We estimated these models using linear regression with a robust estimator of the standard errors [17]. We elected to use observations starting in July 1995 – 3 months after the introduction of the LCA policy, to May 1999, the end of the sample period. The rationale for the choice of starting date was that the LCA (generic substitution) policy had substantive effects on the amount of Pharmacare reimbursed per DDD and hence Pharmacare expenditures. Using post LCA data obviated the need to model the effect of LCA on expenditures. The shortrun and longrun effects of RP (and their standard errors) on Pharmacare drug expenditures were estimated directly from the parameter estimates. To estimate savings using the models of RP on average monthly Pharmacare expenditures per defined daily dose, we first estimated the effect of RP on the change in average monthly Pharmacare expenditures per defined daily dose and then multiplied this change by the monthly number of defined daily doses dispensed (starting with the RP announcement month). We produced separate estimates of the shortrun and longrun effects of RP on Pharmacare drug costs. We also determined the annualized savings estimates of RP, and compared these to expenditures in the year prior to RP to assess the budgetary impact of RP.

We modeled patient-paid expenditures on each of the 3 drug categories, and for all 3 drug categories combined, as a function of an indicator variable equal to one for the periods RP was in effect. Using data beginning with the introduction of LCA, the Pharmacare policy that first introduced patient charges on drug ingredient cost, and ending in May 1999, we estimated the models using linear regression with a robust estimator of the standard errors

3.4.2 *Mortality and admission to longterm care facilities*

We modeled how exposure to RP affects the probability of CVD-related mortality and time to admission to a long-term care facility using the Cox proportional hazards model and, when

necessary, other fully parametric hazard models. We modeled the hazard of both events as a function of an indicator of RP exposure and a set of other patient level characteristics included to control for baseline morbidity variables correlated with RP exposure, which were already described. The output from the models is a hazard ratio – the probability of death (or admission to LTC) of those potentially exposed to RP as a fraction of the probability of death (or admission to LTC) for those not exposed.

The Cox proportional hazards (PH) function $\lambda(t)$ is the product of two components: the baseline hazard function, which depends on the time elapsed since RP (t), denoted $\lambda_0(t)$ and a component which depends on the explanatory variables other than time, $\lambda_i = \exp(\mathbf{x}_i^T \boldsymbol{\beta})$ where \mathbf{x}_i is the vector of characteristics specific to subject i (the exponentiation of the index function $\mathbf{x}_i^T \boldsymbol{\beta}$ ensures that the hazard is non-negative). The Cox model is appropriate when changes in patient characteristics simply shift the entire hazard function up and down, but do not otherwise change its slope. In other words, the Cox model works when the effects of patient characteristics on the instantaneous probability of death does not depend on how long the subject has already survived post RP. This assumption simplifies estimation, and eliminates the necessity to specify the shape of the baseline hazard function, but may be inappropriate in the present model if the effects of RP on mortality operate with a lag.

To ensure that the proportional hazards assumption was indeed consistent with the data, we visually inspected plots of the cumulative hazards for both exposed and comparator groups (if the PH assumption is valid, the hazard curves should not cross), and conducted the test proposed by Grambsch and Therneau [18]. Grambsch and Therneau propose an estimator of the time-specific value of $\boldsymbol{\beta}$, denoted as $\boldsymbol{\beta}(t)$. A finding that $\boldsymbol{\beta}(t)$ is time-invariant lends support to the PH assumption. In the event of a rejection of the PH assumption, we estimated a Generalized Gamma regression model. This model relaxes the PH assumption and nests as special cases the Weibull, exponential and log-log survival models. The output from this model is an estimate of the mean ratio of survival time (in weeks) of those exposed to RP relative to those not exposed.

3.4.3 *Morbidity and non-pharmacological health care costs*

We assembled subject and month specific data on the following variables:

- number of physician consultations outside of hospital
- number of physician emergency or hospital visits
- number of CVD-related surgical procedures
- number of CVD-related diagnostic procedures

- number of hospital admissions for CVD and renal related conditions
- number of days spent in hospital for CVD and renal related conditions
- number of revascularizations (CABG + PTCA) performed in hospital

- number of prescriptions dispensed for sublingual nitroglycerin

For nitrates users, the data covered the period May 1994 to March 1998 (the 18 month period prior to the RP of nitrates in November 1995 and 29 months afterwards). For ACE inhibitor and

CCB users, we used the period July 1995 to March 1998 (the 18-month period prior to the RP of ACE inhibitor and CCBs in January 1997 and the 15-month period afterwards). Observations on physician services and hospitalizations before the first observation of use of any publicly funded health care (the earlier of the first hospital admission and the first physicians billing) were censored, as were observations after the subject died, or if the patient was not observed to die, after the later of the last drug dispensal, hospital admission or physician service. We censored observations on drug dispensing before the subject became eligible for Pharmacare seniors (Plan A) drug benefits. This date was the later of their 65th birthdate, and the date of the first hospital admission or physician service; this rule was imposed to identify those that immigrated to BC after turning 65. Observations on drug dispensing were left-censored using the same method as for physicians and hospitals services.

We used fully parametric estimators to assess the effects of RP on outcomes. These included the fixed effects poisson [19;20], fixed effects linear regression [21] and fixed effects logit estimators [22] as implemented in Stata 7.0 [23]. Each of these models automatically control for subject specific fixed effects. We included indicators of each (monthly) time period to control for time-varying effects common to both exposed and comparator groups, and also included indicator variables to control for the shortrun and longrun effects of RP. The shortrun RP indicator was equal to 1 for observations on the potentially exposed group for the first 4 months post policy and equal to zero otherwise. The longrun indicator was equal to 1 for observations on the potentially exposed group for all months after the introduction of RP and equal to zero otherwise. All of the morbidity outcomes are non-negative counts, for which the poisson model is particularly appropriate. The RP parameter estimates were expressed as ‘incidence rate ratios’ – the number of events conditional on exposure to RP (both in the shortrun and longrun) as a fraction of the number of events conditional on no exposure to RP. We also used the fixed effects estimator for comparison purposes, although its standard errors are potentially heteroskedastic. Given that the number of events per subject and month for some outcomes, such as hospitalizations per month, were usually small, we redefined the outcome variable to be the probability that *any* event was observed per month (e.g. the probability that the subject was hospitalized for a CVD-related condition in a particular month) and estimated via the fixed effects logit model.

3.4.4 *Probability of exemption and amount paid out of pocket*

Logit regression was used to estimate the effect of low income status on the probability of continuous exemption from RP; a ‘two part’ regression model was used to estimate the effect of low income status on the amount paid in the subsample of those not exempted from RP. Logit regression was used to estimate the probability that the patient paid over \$1 for Restricted drugs in the year following the introduction of RP. Linear regression was then used to estimate the amount paid in the subsample of those paying over \$1. We estimated linear regression models for both the actual amount paid and the logarithm of the amount paid. The former model estimates the *absolute* dollar difference in payment between subjects with low vs. high income status, while the latter model estimates the *relative* difference in the amount paid between the 2 groups. Heteroskedasticity robust standard error estimators were used in all models [17].

4 RESULTS

4.1 Effects of RP on drug use and drug costs aggregated across all seniors

We summarize pre-post RP trends in the use and costs of the Restricted and Unrestricted nitrates, ACE inhibitors and CCBs, as well as substitutes for these drugs, using Pharmacare claims data aggregated across all seniors. Table 8 below summarizes the mean monthly number of defined daily doses of nitrate drugs and substitutes (beta blockers and CCBs) dispensed over time periods before and after the introduction of the Low Cost Alternative program in April 1994, the introduction of nitrates RP in November 1995, the removal of the 0.2 and 0.4 mg nitroglycerin patches from the RP policy in February 1996,²⁵ and the introduction of RP for the CCBs in January 1997. Included in the table is an index of each period's mean monthly DDDs dispensed relative to the mean monthly DDDs dispensed in the period directly preceding the introduction of nitrates RP, April 1994 - October 1995. The monthly DDDs of various nitrates, grouped by their RP reimbursement status, are graphed in Figure 3.

The introduction of RP to the nitrate drugs was associated with large changes in the types of nitrate drugs dispensed: in September 1995, possibly anticipating the upcoming RP policy, seniors stockpiled the two most commonly used Restricted nitrates – the NTG Patch and the SR NTG tablets. Use of these drugs dropped dramatically after RP was implemented, and at the same time the use of the Unrestricted nitrates, isosorbide dinitrate in particular, increased markedly. The use of the reference standard products increased to 277% of their pre RP levels while the use of the restricted products decreased to 35% of their pre RP levels and the use of the nitroglycerin patch decreased to 68% of its pre RP level. After the 0.2 and 0.4 mg strengths of the patch were removed from RP, however, the rates of patch dispensing quickly returned to its pre-policy level and rate of growth. Use of ISDN meanwhile gradually dropped and use of SR NTG, whose remuneration was still restricted under the policy, remained well below its pre-RP levels. The use of the sublingual nitroglycerin did not appear to change after the policy. The overall rates of use of nitrates appeared to drop slightly after the policy – the post-policy DDDs of all nitrates are slightly below what we would have expected, based on pre-RP trends (Figure 9). Graphs of the trends in volume of CCBs (Figure 9) and beta blockers (Figure 11) did not, however, reveal any substantive increases in the use of these potential substitutes for nitrates after the introduction of nitrates RP.

Average Pharmacare reimbursement per DDD of the patch (not including drug dispensing fees), and the reference standard nitrates (in particular ISDN) dropped after the introduction of the LCA policy (Figure 4 and Table 9). The reimbursement of the patch dropped after the RP policy was initiated and again declined after the manufacturers voluntarily reduced prices. Reimbursement of the SR NTG initially dropped post RP, but then rose; the rise is likely due to the increased rates of special authority exemption for this drug post RP. Rates of reimbursement of the sublingual nitrates gradually rose over time as well. On balance, RP substantially reduced the average Pharmacare reimbursement per DDD of all nitrates (Figure 8).

²⁵ The 0.2 and 0.4 mg nitroglycerin patch was actually removed from RP in the 3rd week of January 1996. Given that RP was in effect for most of January, we used February as the effective introduction date.

The net effect of the nitrates RP policy was to reduce Pharmacare expenditures: Pharmacare spent slightly more on the Unrestricted nitrates, but this was more than offset by lower expenditures on the SR and patch formulations (Figure 5 and Table 10). No compensatory increases in Pharmacare spending on the beta blockers or CCBs were apparent. While most of Pharmacare savings are attributable to the lower prices paid for the patch and SR NTG, some of the savings represented increased expenditures by seniors who elected to pay out of pocket the difference between the retail price of the Restricted drugs and the Pharmacare subsidy (Figure 6 and Table 11). Most of the payment was made when the policy was first introduced – rates of patient expenditures dropped dramatically thereafter.

Figure 7 displays the total Pharmacare expenditures on nitrates before and after the policy and presents a forecast of what expenditures would have been, had RP not been introduced. We estimated that RP of nitrates reduced Pharmacare spending by \$3,750,000 per year (95% CI: \$3.3 to \$4.2 million) (Table 5). This saving represents 52% of the amount that Pharmacare spent on nitrates in the year prior to the announcement of RP. Part of the reason that spending on nitrates was lower post-RP is due to slight declines in the number of DDDs of nitrates dispensed. If we assume that this reduction in consumption was not due to RP, we get a lower estimate of savings: \$2,950,000 (95% CI: \$2.7 to \$3.2 million). Table 6 displays estimates of the effect of RP on patient paid expenditures on nitrates, ACE inhibitors and CCBs. We estimate that patients contributed under \$1 million over the 44 months after the introduction of the policy in October 1995 to the end of the sample period, May 1999. This translates into an annualized contribution of \$264,000 (95% CI: \$194,000 to \$334,000), and represents approximately 7% to 9% of Pharmacare savings, depending on the savings estimate used.

Table 5 Estimated savings to Pharmacare attributable to RP (with 95% confidence intervals), by drug group and estimation method.

Drug Group	Model of Effect of RP on:	Short-term Savings			Long-term Savings to May 1999		
		Estimate	95% Confidence Int.		Estimate	95% Confidence Int.	
Nitrates	Pharmacare reimbursement per defined daily dose	-271,061	-944,954	402,832	11,300,000	10,800,000	11,900,000
	Total expenditures	-458,163	-1,480,671	564,346	14,500,000	13,300,000	15,700,000
ACE inhibitors	Pharmacare reimbursement per defined daily dose	-988,548	-1,592,297	-384,799	4,078,380	561,771	7,594,990
	Total expenditures	46,170	-1,025,976	1,118,316	-270,258	-4,036,414	3,495,899
CCBs	Pharmacare reimbursement per defined daily dose	-611,073	-1,657,002	434,857	10,200,000	7,727,590	12,600,000
	Total expenditures	-585,050	-2,303,652	1,133,551	11,500,000	7,589,838	15,400,000
Totals	Pharmacare reimbursement per defined daily dose	-1,870,682			25,578,380		
	Total expenditures	-997,043			25,729,742		
Drug Group	Model of Effect of RP on:	Total Savings to May 1999			Annualized Total Savings		
		Estimate	95% Confidence Int.		Estimate	95% Confidence Int.	
Nitrates	Pharmacare reimbursement per defined daily dose	11,100,000	10,100,000	12,000,000	2,949,740	2,700,276	3,199,204
	Total expenditures	14,100,000	12,400,000	15,700,000	3,748,791	3,299,969	4,197,613
ACE inhibitors	Pharmacare reimbursement per defined daily dose	3,089,832	-261,802	6,441,466	1,158,687	-98,176	2,415,550
	Total expenditures	-224,088	-3,846,125	3,397,949	-84,033	-1,442,297	1,274,231
CCBs	Pharmacare reimbursement per defined daily dose	9,574,425	7,126,907	12,000,000	3,590,410	2,672,590	4,508,229
	Total expenditures	10,900,000	6,901,709	14,900,000	4,086,443	2,588,141	5,584,746
Totals	Pharmacare reimbursement per defined daily dose	23,764,257			7,698,837		
	Total expenditures	24,775,912			7,751,201		

Note: these estimates represent savings on the drugs dispensed to seniors only. Any savings on dispensing fees due to the filling of fewer prescriptions are not included, nor are savings attributable to the application of RP to other Pharmacare beneficiary groups. Short term effects of RP captures changes in Pharmacare expenditures during the period starting with the announcement of the policy and ending 3 months after the introduction of the policy. Long term effects capture changes in Pharmacare expenditures starting with the announcement of the policy, and ending at the end of the sample period (May 1999). We estimated the effect of RP on total Pharmacare expenditures directly and also estimated the effect of RP on Pharmacare reimbursement per defined daily dose, assuming that RP had no effect on the total volume of drugs dispensed.

Table 6 Estimated patient expenditures on Restricted drugs attributable to RP (with 95% confidence intervals), by time period and drug group.

Drug Group	Time Period	Estimated Patient Expenditures	95% Confidence Interval	
Nitrates	RP introduction to May 1999	969,431	711,397	1,227,465
	Annualized	264,390	194,017	334,763
ACE inhibitors	RP introduction to May 1999	2,175,115	2,037,633	2,312,596
	Annualized	900,048	843,159	956,937
CCBs	RP introduction to May 1999	1,870,715	1,686,708	2,054,723
	Annualized	774,089	697,948	850,230
Totals	RP introduction to May 1999	5,827,756	5,246,348	6,409,165
	Annualized	2,014,516	1,843,617	2,185,415

Table 12 summarizes the mean monthly number of defined daily doses of ACE inhibitor & CCB drugs and substitutes (beta blockers, alpha blockers, AT2s, central acting medications & vasodilators, and diuretics) dispensed over the time periods before and after the announcement of RP (late October 1996), the introduction of RP (January 1997), the month following the period of implementation and adjustment to RP (April 1997) and a follow-up period (starting April 1998). After RP was applied to the ACE inhibitors, both the level and rate of growth in the use of the Restricted ACE inhibitors (enalapril in particular) fell, whereas the use of the Unrestricted ACE inhibitors (in particular ramipril and to a lesser extent quinapril) grew sharply, and more than compensated for lower use of the Restricted ACE inhibitors (Figure 10). In fact use of all types of ACE inhibitors grew 50% per capita from the baseline period (October 1995 - September 1996) to the period April 1998 - May 1999. There did not appear to be any disruptions in the prescribing trends for potential substitutes to ACE inhibitors after the introduction of RP (Figure 11).

The average Pharmacare reimbursement per DDD of both the Restricted ACE inhibitors (Figure 12) and all ACE inhibitors (Figure 8) fell slightly after the introduction of RP, but this decline was nowhere near the declines observed for the nitrates. There are two possible explanations: first, many seniors could have been exempted from the RP policy, in which case Pharmacare continued to reimburse these drugs as before the policy. Another explanation is due to the fact that the reference price for ACE inhibitors was set relatively high (see Table 2). Hence a beneficiary using a low dose of a Restricted drug could still be completely covered. To investigate this, we examined the patient-level prescribing records of those who filled at least 1 prescription of enalapril (the most commonly prescribed Restricted ACE inhibitor pre-RP) per quarter, and identified subjects whose monthly drug ingredient cost was less than the reference price of \$27. We found that during the first quarter of 1997 – the quarter that RP of ACE inhibitors was introduced – over 45% of users had drug costs under the reference price (Table 7).

The net effect of the changes in ACE inhibitor reimbursement and drug use produced relatively small savings to Pharmacare. As is displayed in Figure 13 and Table 13, the increase in expenditures on Reference Standard ACE inhibitors was almost equal to the drop in expenditures on Restricted ACE inhibitors. The estimated savings Pharmacare realized from applying RP to

these drugs depends critically on whether the rapid increase in the rates of use of ACE inhibitors (especially ramipril and quinapril) post RP would have happened even without RP. Using the estimating method that assumes that RP was responsible for the prescribing growth yields a small *negative* annualized savings of -\$84,032, although the 95% confidence interval (-\$1.4 to +\$1.3 million) is almost exactly centered on zero (Table 5). If, on the other hand, the rapid increases in ACE inhibitor prescribing would have happened even without RP, then annualized total savings are positive – \$1.2 million (95% CI: -\$0.1 to +\$2.4 million) – but still relatively small.

Table 7 Frequency and percentage of Enalapril users 65+ years whose monthly drug cost is below the Reference Price (\$27/month), by quarter: 1995 Q3 – 1998 Q1

Quarter	Statistic	Number and % above Ref Price	Number and % Below Ref. Price	Total
95 3	Frequency	7,406	6,805	14,211
	Percentage	52.11	47.89	100
95 4	Frequency	7,474	7,651	15,125
	Percentage	49.41	50.59	100
96 1	Frequency	8,156	7,986	16,142
	Percentage	50.53	49.47	100
96 2	Frequency	9,211	8,380	17,591
	Percentage	52.36	47.64	100
96 3	Frequency	11,310	6,063	17,373
	Percentage	65.10	34.90	100
96 4	Frequency	12,738	4,977	17,715
	Percentage	71.91	28.09	100
97 1 (introduction of RP of ACE/CCB)	Frequency	7,037	5,884	12,921
	Percentage	54.46	45.54	100
97 2	Frequency	7,495	4,776	12,271
	Percentage	61.08	38.92	100
97 3	Frequency	7,101	4,462	11,563
	Percentage	61.41	38.59	100
97 4	Frequency	7,015	4,130	11,145
	Percentage	62.94	37.06	100
98 1	Frequency	6,200	3,917	10,117
	Percentage	61.28	38.72	100
Total	Frequency	91,143	65,031	156,174
	Percentage	58.36	41.64	100

Prior to the introduction of the CCB RP policy, the rate of use of amlodipine was increasing rapidly (Table 12), while the use of the other Restricted CCBs was declining (nifedipine SR was still, however, the most commonly dispensed Restricted CCB before RP). The implementation of RP only exacerbated the pre-existing declines in the use of nifedipine (both RR and SR) and nicardipine. The level of use of amlodipine per 100,000 seniors declined after the policy, but its rate of growth declined only slightly. DDDs of the drug eventually increased 34% over the baseline levels. Dispensing of felodipine, the reference standard CCB, increased gradually after the policy (Figure 10). The restriction on the reimbursement of the SR forms of diltiazem and verapamil caused only a temporary drop in rates of prescribing of all dosage forms of these

drugs. Somewhat surprisingly, the policy did not result in appreciable increases in the rates of prescribing of the RR versions of these drugs, nor were there appreciable decreases in the rates of dispensing of the SR versions. On balance, rates of dispensing of all CCBs declined after RP – and this decline was markedly lower than pre-RP trends would have predicted (Figure 9).

There was substantial variation in Pharmacare reimbursement per DDD of the CCBs after RP was introduced. Reimbursement per DDD of the Exempt CCBs (regular and sustained release diltiazem and verapamil) fell sharply, while somewhat surprisingly the reimbursement of the Restricted CCBs fell only slightly (Figure 12). As expected, reimbursement of felodipine was unaffected by the policy. On balance, however, rates of Pharmacare reimbursement per DDD of all the CCBs combined fell after the policy (Figure 8).

The combination of reduced use and lower reimbursement per DDD of the Restricted CCBs and SR diltiazem and verapamil reduced Pharmacare expenditure on these drugs; these lower expenditures were only partially offset by increased expenditures on felodipine. The net effect of these changes was to lower overall Pharmacare expenditure on CCBs (Table 14 and Figure 13). Assuming that RP was responsible for the declines in the volume of CCBs, we estimate that Pharmacare expenditures on all CCBs dispensed to seniors declined by an average of \$4.1 million per year (95% CI: \$2.6 to \$5.6 million) (Figure 17 and Table 5). Assuming that the decline in CCB use would have occurred even had RP not been introduced reduced estimates of the annualized savings to \$3.6 million per year (95% CI: \$2.7 to \$4.5 million). The lower and higher annualized savings estimates represent 13% and 15%, respectively, of the \$27.2 million Pharmacare spent on CCBs for seniors (not including dispensing fees) during the 12 month period prior to the announcement of RP.

Aggregating annualized Pharmacare savings due to RP of nitrates, ACE inhibitors and CCBs produces annualized savings estimates of \$7.7 million (assuming aggregated drug class prescribing volumes are unaffected by RP) and \$7.8 (assuming aggregated drug class prescribing volumes are affected by RP). Adding up total savings across the three drug classes from the announcement dates of the respective policies to May 1999 yields a total savings estimate of \$23.8 to \$24.8 million, depending on the estimation method used (Table 5).

The rate of patient expenditure on the Restricted ACE inhibitors and CCBs was in the range of \$10,000-\$20,000 per 100,000 seniors per month following the introduction of RP (Figure 15 and Table 15). Just as was observed for the Restricted nitrates, patient expenditures were highest directly after the policy introduction. This was likely because seniors taking these drugs did not have time to consult with their physicians regarding therapy options, and elected to pay to be able to continue using them. Interestingly, unlike the nitrates, where patient payments dropped sharply within a few months of the policy, the rates of patient spending for the Restricted ACE inhibitors and CCBs remained relatively high sometime after the introduction of RP.

Some of the savings from RP represents additional costs assumed by seniors who elected to pay out of pocket for higher priced drugs. Adding up senior-paid drug ingredient cost for Restricted drugs, and SR diltiazem and verapamil across the 3 drug groups, from the introduction of RP to May 1999, yields \$5.9 million, or approximately 24% of the total savings realized by Pharmacare. Of course, some of these expenditures would have been paid due to the LCA and

MPP. But the amounts spent by seniors on LCA and MPP are likely small relative to contributions due to RP: We estimate the additional spending across the 3 drug groups due to the introduction of RP, from the introduction of RP to the end of the sample period, to be \$5.8 million (95% confidence interval: \$5.2 to \$6.4 million) (Table 6).

Figure 3 Defined daily doses of Nitrate drugs dispensed per 100,000 seniors, by reimbursement status and month

Note: LCA indicates the introduction of the Low Cost Alternative program, RP Nitrates indicates the introduction of the nitrates Reference Pricing program and RP ACE/CCB indicates the introduction of the ACE inhibitor & Calcium Channel Blocker Reference Pricing program.

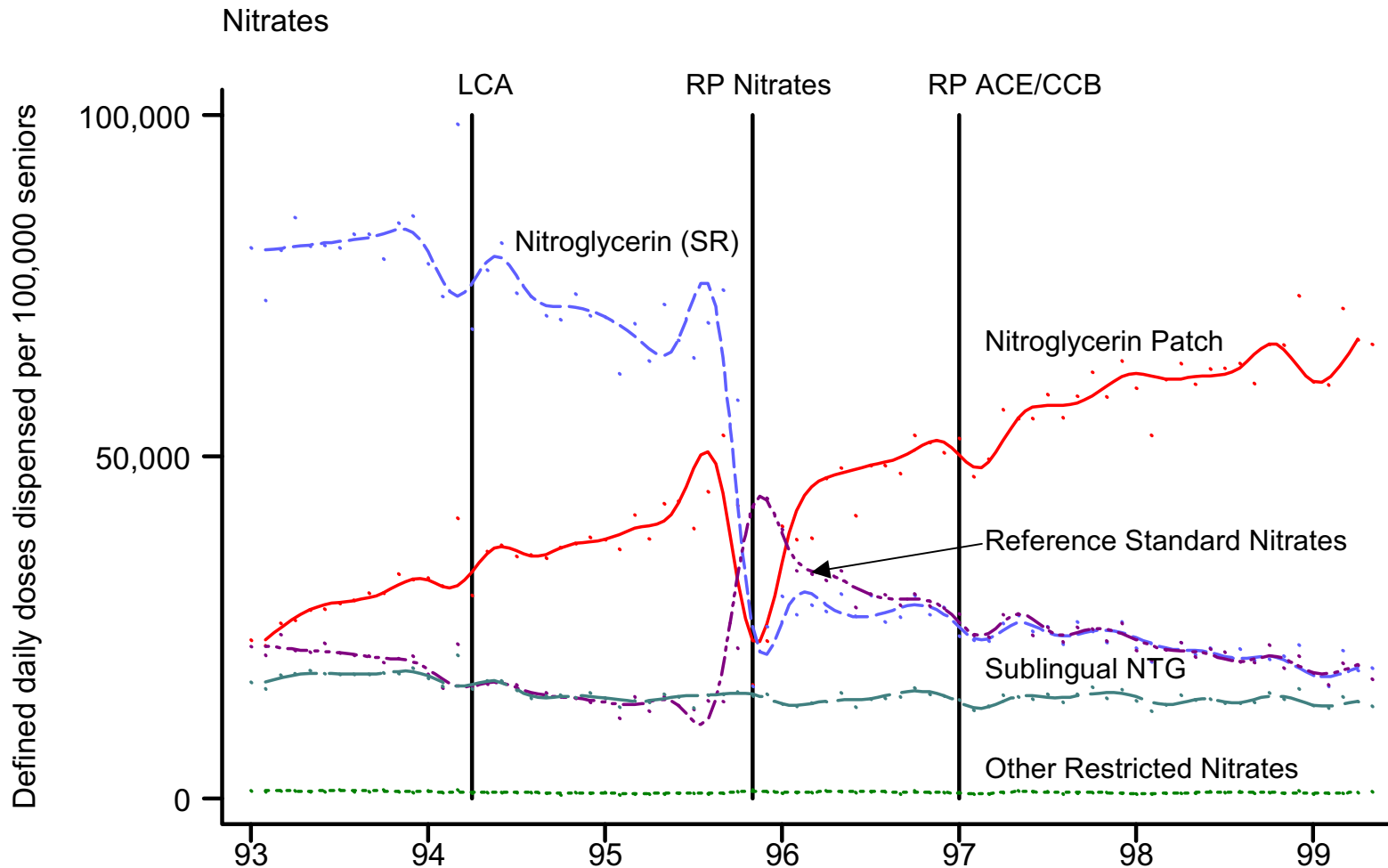


Figure 4 Pharmacare reimbursement per defined daily dose of Nitrate drugs, by reimbursement status and month

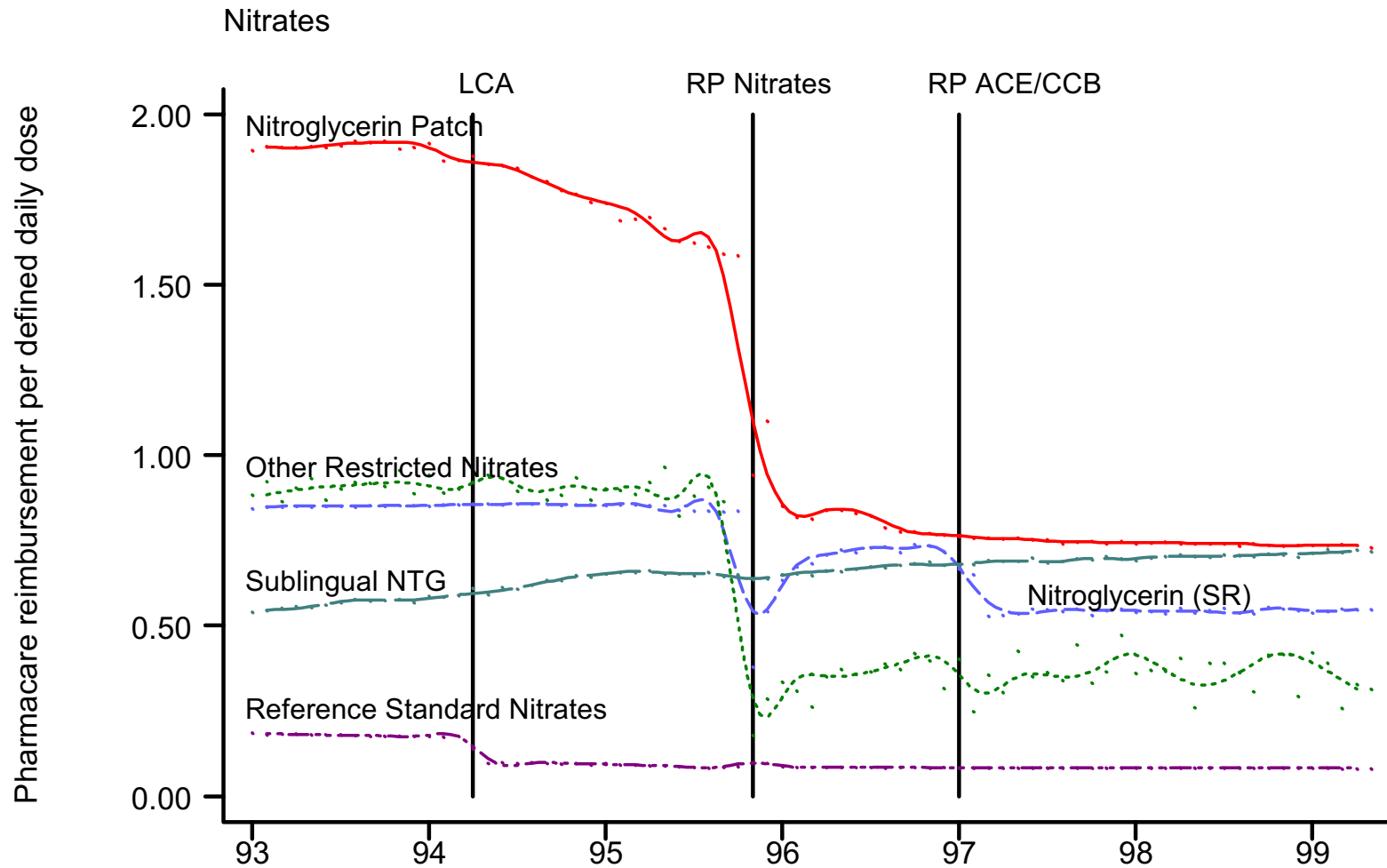


Figure 5 Pharmacare ingredient cost expenditures on Nitrate drugs dispensed per 100,000 seniors, by reimbursement status and month

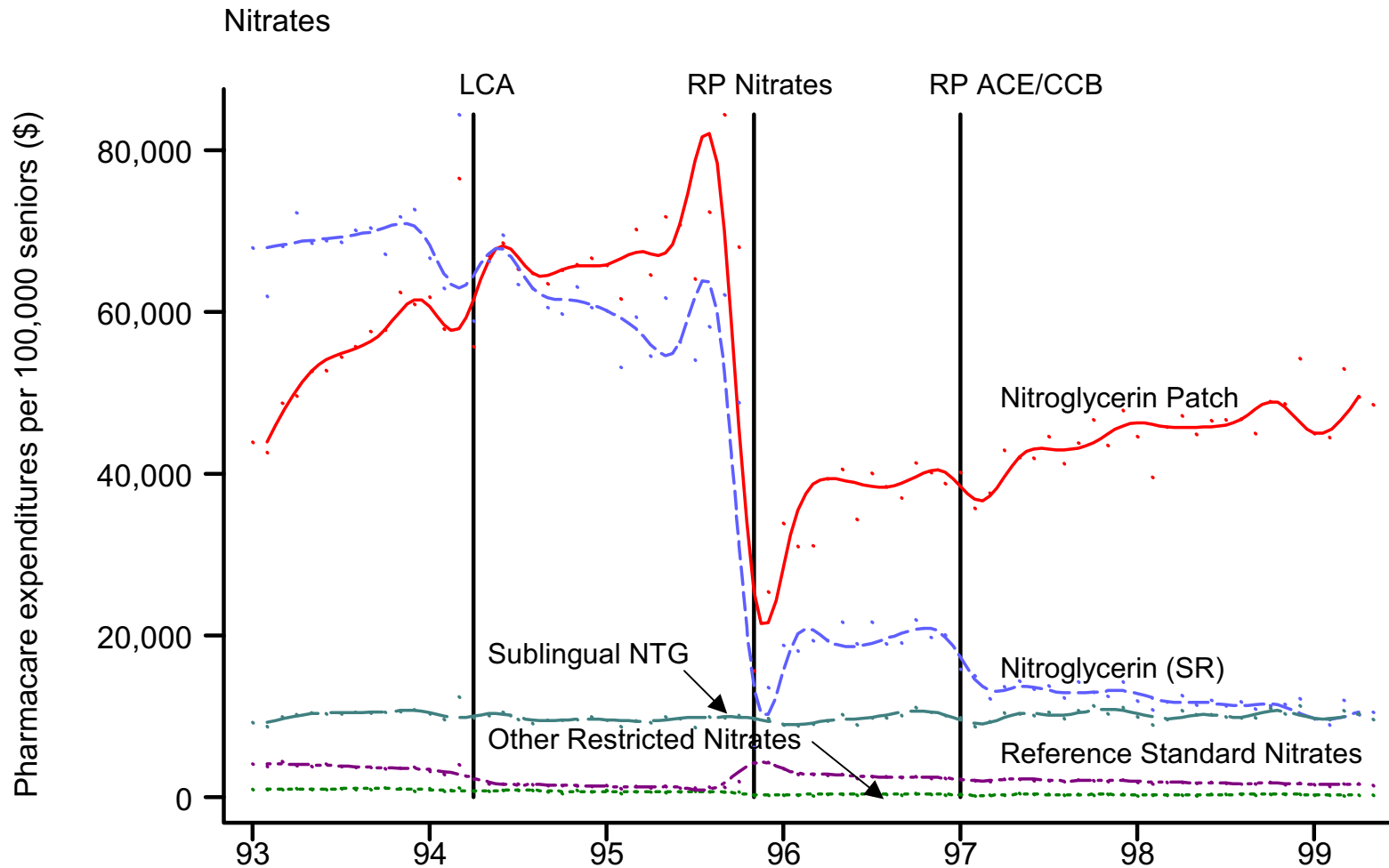


Figure 6 Patient ingredient cost expenditures on Nitrate drugs dispensed per 100,000 seniors, by reimbursement status and month

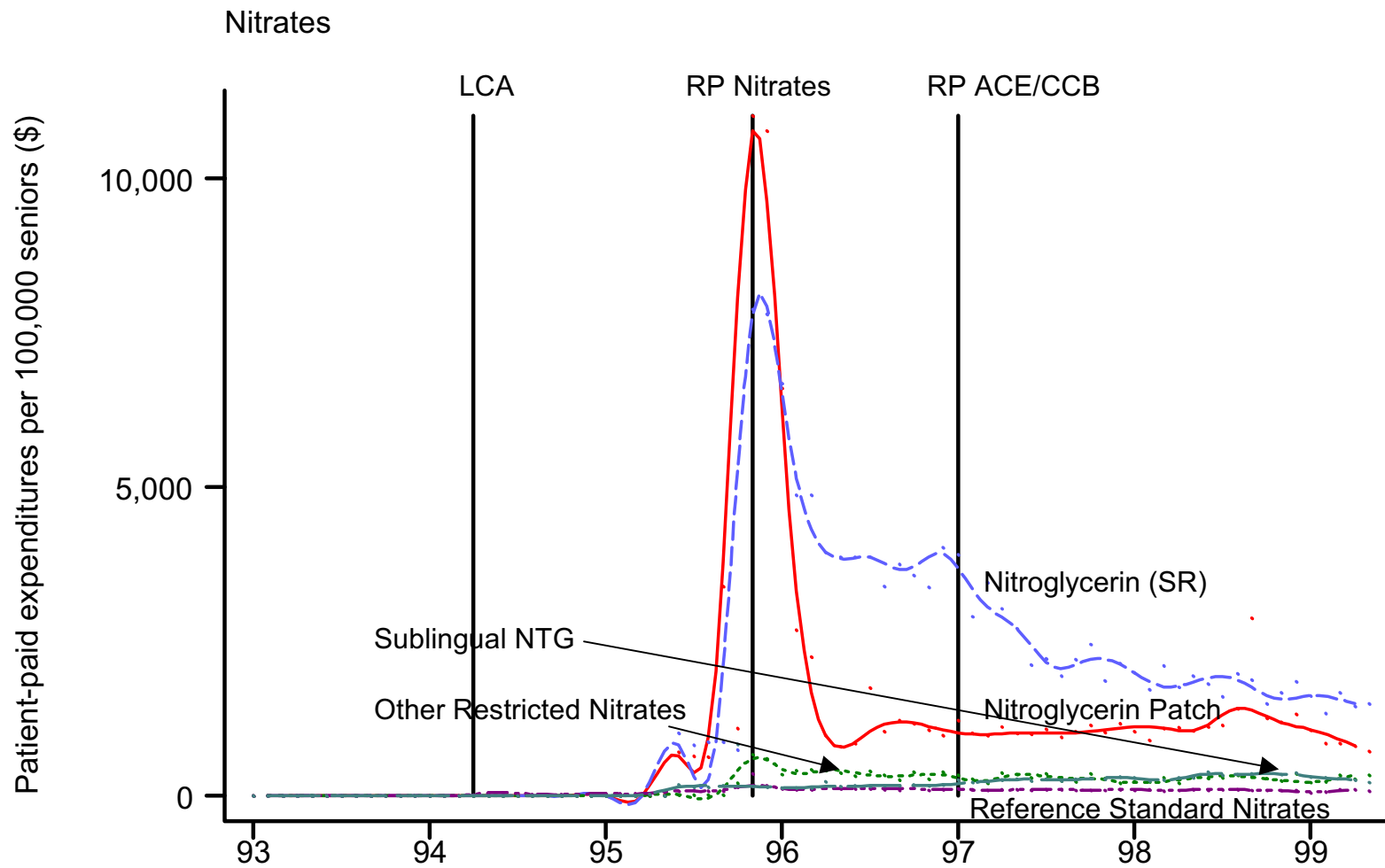


Figure 7 Actual and predicted Pharmacare expenditures on Nitrates with and without RP, per 100,000 seniors, by month, with 95% confidence intervals

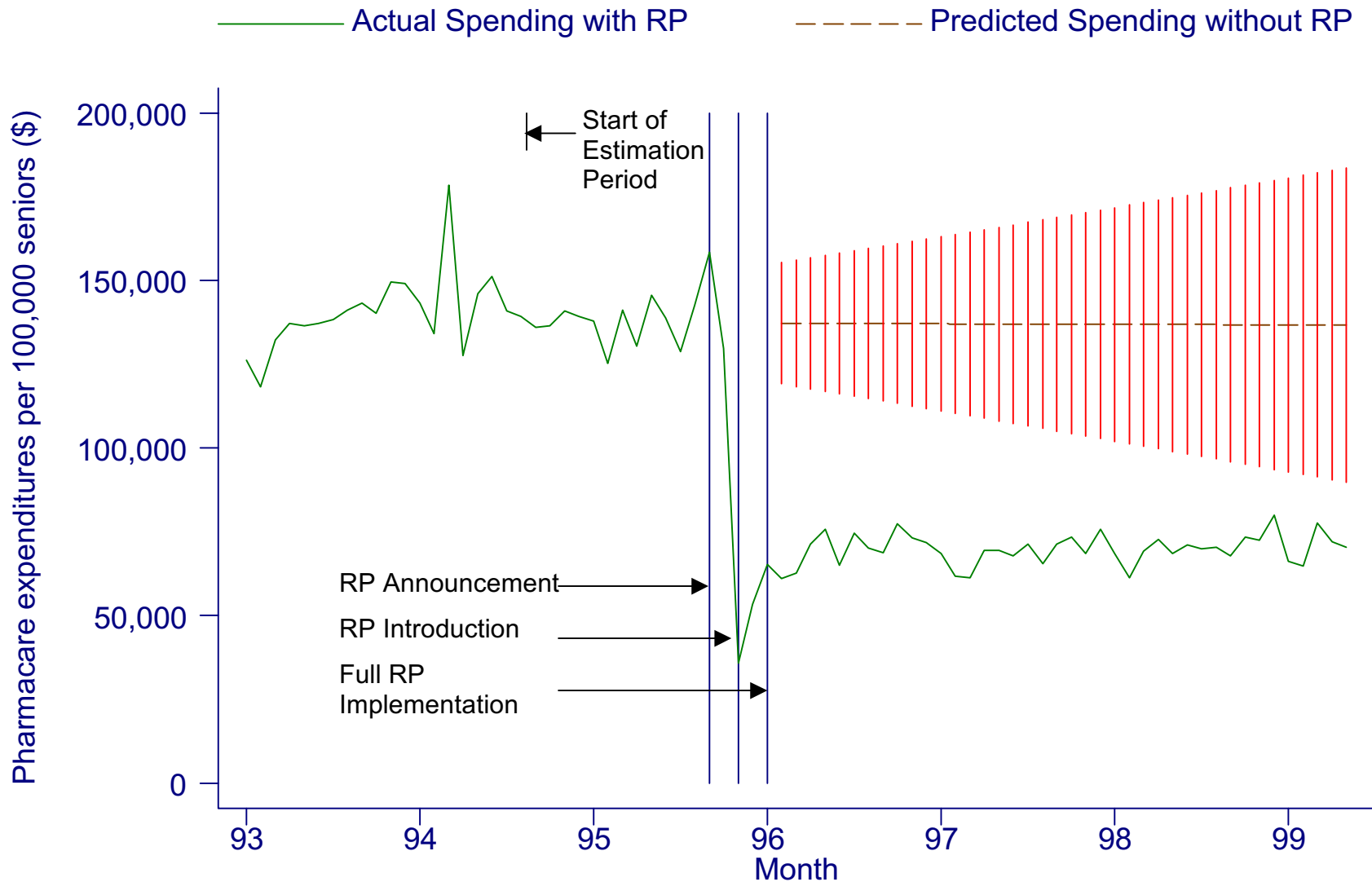


Figure 8 Pharmacare reimbursement per defined daily dose of Nitrates, ACE inhibitors and CCBs, by month.

Trend lines, estimated using data 3 months post-LCA up to the month prior to the announcement of RP, are displayed to indicate what might have happened to Pharmacare reimbursement had RP not been introduced.

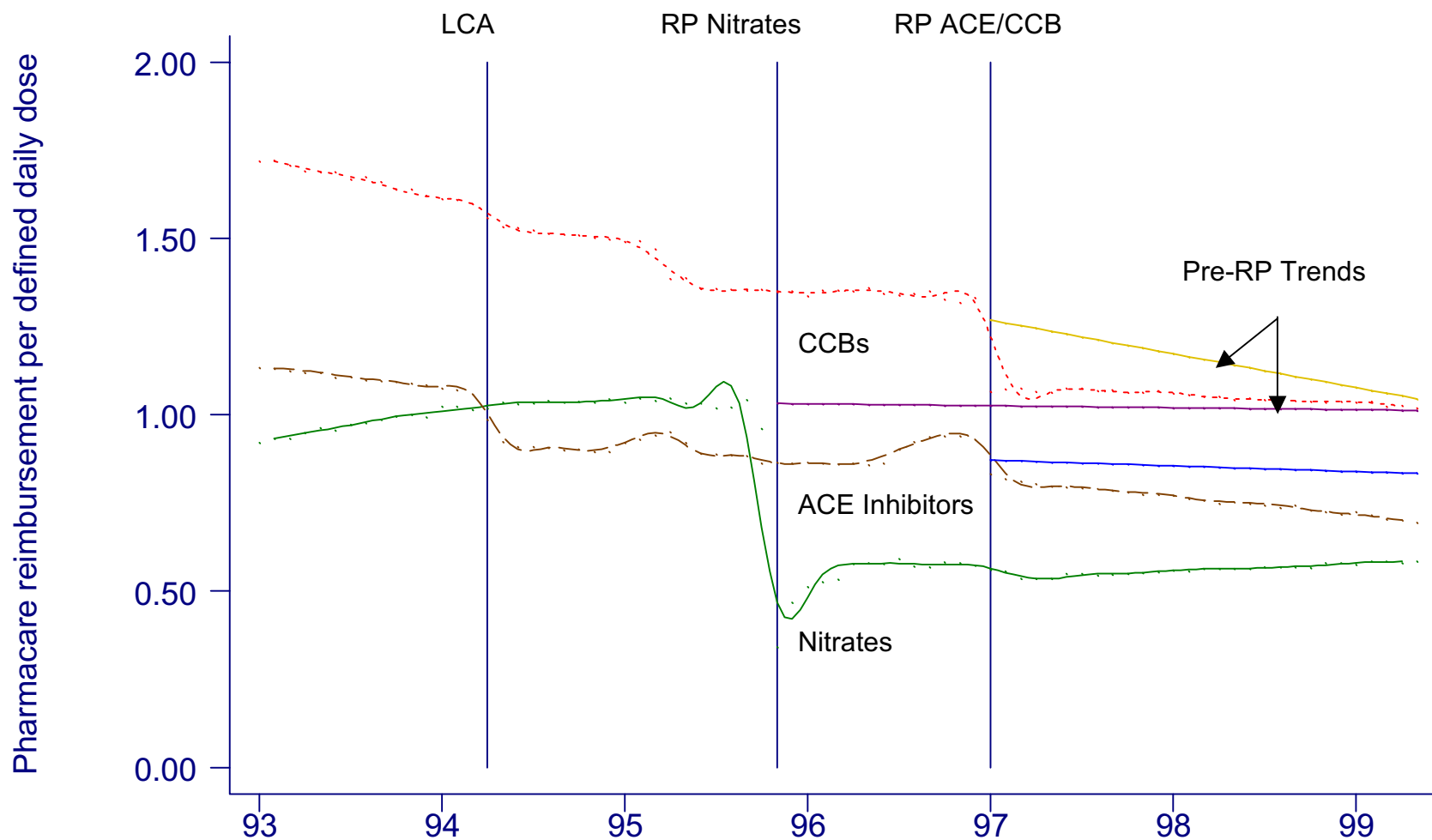


Figure 9 Number of defined daily doses of Nitrates, ACE inhibitors and CCBs dispensed per 100,000 seniors, by month.

Trend lines, estimated using data 3 months post-LCA up to the month prior to the announcement of RP, are displayed to indicate what might have happened to prescribing volumes had RP not been introduced

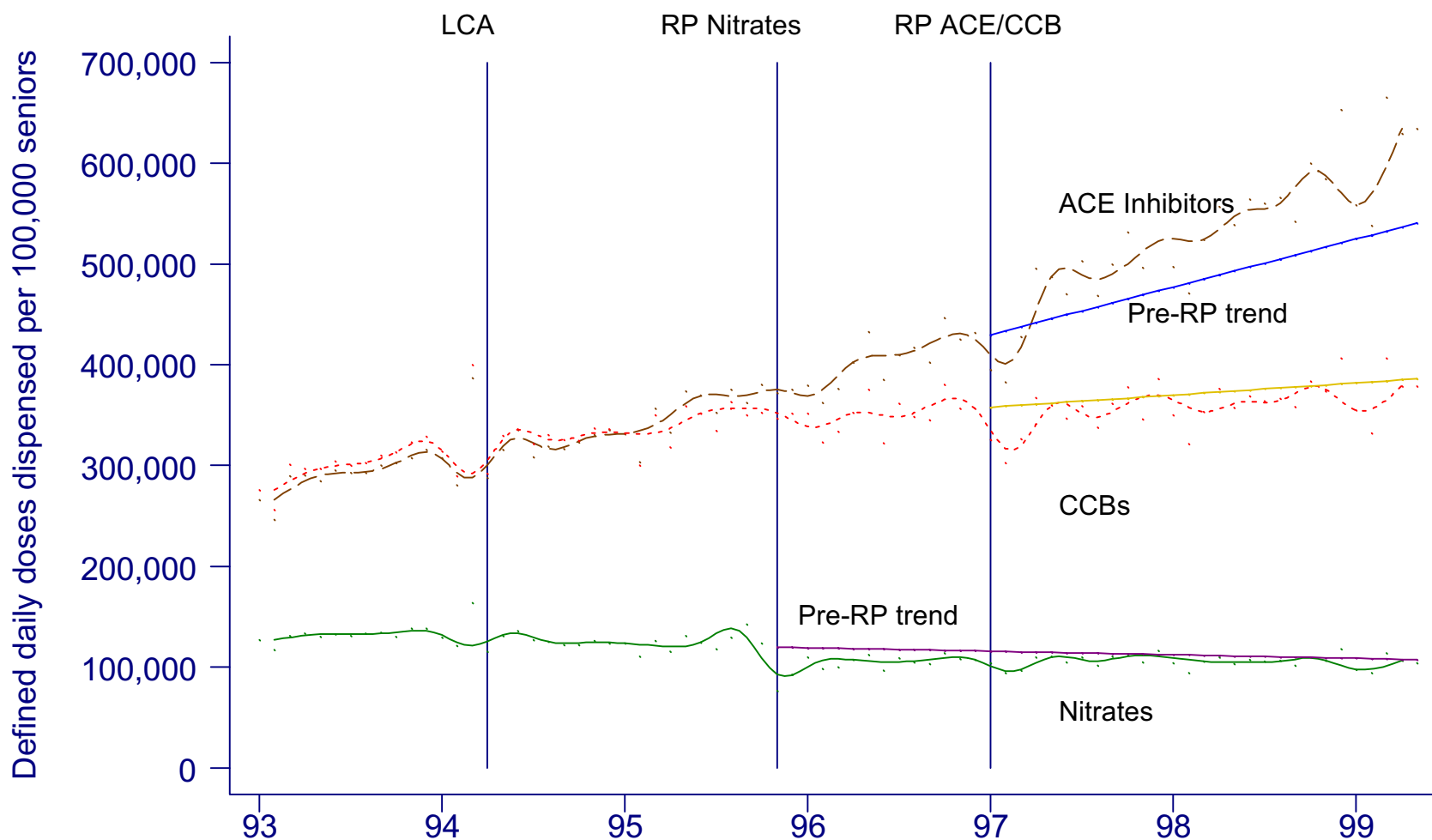


Table 8 Mean number of defined daily doses dispensed per 100,000 senior Pharmacare beneficiaries per month, by cardiovascular drug type and policy period – nitrate drugs and substitutes

Highlighted in bold is an index of each period's mean monthly DDDs dispensed relative to the mean monthly DDDs dispensed in the period directly preceding the introduction of nitrates RP, April 1994 - October 1995.

		Pre-LCA Jan 93 - Mar 94	LCA Policy Apr 94 - Oct 95	RP of Nitrates Nov 95 - Jan 96	NTG Patch Exempted Feb 96 - Dec 96	RP of CCBs Jan 97 - May 99
NITRATES						
<i>Restricted</i>	NTG (SR)	81,679 117	70,109 100	23,710 34	27,832 40	22,220 32
	Pentaerythritol	464 140	331 100	149 45	125 38	85 26
	Iso. Mononitrate	0	24 100	324 1,350	282 1,175	262 1,092
	Iso. Mononitrate (SR)	0	175 100	428 245	429 245	470 269
	Iso. Dinitrate (SR)	641 142	453 100	138 30	113 25	51 11
<i>All Restricted Nitrates</i>		82,784 116	71,092 100	24,749 35	28,781 40	23,088 32
<i>Ref. Standard</i>	Iso. Dinitrate	19,908 136	14,688 100	39,086 266	29,968 204	22,048 150
	NTG Ointment	1,072 233	460 100	2,935 638	360 78	178 39
	<i>All Ref. Std. Nitrates</i>	20,980 139	15,148 100	42,021 277	30,328 200	22,226 147
<i>Variable</i>	NTG Patch	29,310 75	39,075 100	26,494 68	46,693 119	60,652 155
<i>Exempt</i>	NTG Sublingual	18,122 120	15,119 100	14,701 97	14,679 97	14,489 96
<i>All Nitrates</i>		151,196 108	140,434 100	107,965 77	120,481 86	120,455 86
CALCIUM CHANNEL BLOCKERS						
<i>Restricted</i>	Nifedipine	8,986 153	5,887 100	4,938 84	2,785 47	136 2
	Nifedipine (SR)	116,621 96	121,497 100	122,612 101	112,536 93	91,725 75
	Nicardipine	2,621 145	1,805 100	1,398 77	1,148 64	642 36
	Amlodipine	12,660 39	32,265 100	47,888 148	62,745 194	66,303 205
	<i>All Restricted CCBs</i>	140,888 87	161,454 100	176,836 110	179,214 111	158,806 98
<i>Ref. Standard</i>	Felodipine	23,216 64	36,054 100	41,585 115	42,458 118	80,144 222
<i>Exempt</i>	Diltiazem	20,452 153	13,360 100	10,082 75	7,934 59	4,865 36
	Diltiazem (SR)	80,111 97	82,374 100	81,743 99	81,371 99	77,859 95
	Verapamil	12,327 131	9,407 100	7,986 85	6,916 74	5,470 58
	Verapamil (SR)	30,708 98	31,389 100	32,098 102	32,699 104	32,408 103
	<i>All Exempt CCBs</i>	166,814 97	172,584 100	173,494 101	171,378 99	200,746 116
<i>All CCBs</i>		330,918 89	370,092 100	391,915 106	393,050 106	439,696 119
BETA BLOCKERS						
<i>Exempt</i>		184,608 101	182,632 100	192,113 105	199,754 109	221,653 121

Table 9 Mean Pharmacare reimbursement price per Defined Daily Dose, by cardiovascular drug type and policy period – nitrate drugs and substitutes

Highlighted in bold is an index of each period's mean monthly Pharmacare reimbursement per DDDs dispensed relative to the mean monthly DDDs dispensed in the period directly preceding the introduction of nitrates RP, April 1994 - October 1995.

		Pre-LCA Jan 93 - Mar 94	LCA Policy Apr 94 - Oct 95	RP of Nitrates Nov 95 - Jan 96	NTG Patch Exempted Feb 96 - Dec 96	RP of CCBs Jan 97 - May 99
NITRATES						
<i>Restricted</i>	NTG (SR)	0.85 100	0.85 100	0.54 64	0.72 85	0.55 65
	Pentaerythritol	0.66 94	0.70 100	0.30 43	0.48 69	0.52 74
	Iso. Mononitrate			0.26	0.36	0.47
	Iso. Mononitrate (SR)		0.10 100	0.15 150	0.17 170	0.22 220
	Iso. Dinitrate (SR)	1.09 104	1.05 100	0.55 52	0.95 90	0.90 86
<i>All Restricted Nitrates</i>		0.85 100	0.85 100	0.53 62	0.70 83	0.54 64
<i>Ref. Standard</i>	Iso. Dinitrate	0.17 189	0.09 100	0.08 89	0.08 89	0.08 89
	NTG Ointment	0.28 108	0.26 100	0.26 100	0.26 100	0.26 100
	<i>All Ref. Std. Nitrates</i>	0.18 187	0.10 100	0.10 100	0.09 89	0.08 87
<i>Variable</i>	NTG Patch	1.90 110	1.72 100	0.94 55	0.80 47	0.74 43
<i>Exempt</i>	NTG Sublingual	0.57 89	0.64 100	0.64 100	0.67 105	0.70 109
<i>All Nitrates</i>		0.93 94	0.99 100	0.48 48	0.58 59	0.58 59
CALCIUM CHANNEL BLOCKERS						
<i>Restricted</i>	Nifedipine	1.24 177	0.70 100	0.69 99	0.67 96	0.64 91
	Nifedipine (SR)	1.14 111	1.03 100	0.92 89	0.91 88	0.88 85
	Nicardipine	2.65 101	2.63 100	2.39 91	2.32 88	2.15 82
	Amlodipine	1.30 107	1.22 100	1.20 98	1.23 101	1.12 92
	<i>All Restricted CCBs</i>	1.19 111	1.07 100	1.00 93	1.03 96	0.99 92
<i>Ref. Standard</i>	Felodipine	0.64 100	0.64 100	0.64 100	0.64 100	0.62 97
<i>Exempt</i>	Diltiazem	2.41 147	1.64 100	1.60 98	1.60 98	1.57 96
	Diltiazem (SR)	2.64 104	2.54 100	2.37 93	2.37 93	1.63 64
	Verapamil	1.59 167	0.95 100	0.89 94	0.89 94	0.86 91
	Verapamil (SR)	1.56 99	1.58 100	1.56 99	1.44 91	0.98 62
	<i>All Exempt CCBs</i>	2.29 108	2.12 100	2.03 96	2.01 95	1.42 67
<i>All CCBs</i>		1.66 114	1.45 100	1.35 93	1.34 92	1.05 72
BETA BLOCKERS						
<i>Exempt</i>		0.84 111	0.76 100	0.71 93	0.67 88	0.65 86

Table 10 Mean Pharmacare-reimbursed drug expenditures per 100,000 senior Pharmacare beneficiaries per month, by cardiovascular drug type and policy period – nitrate drugs and substitutes

Highlighted in bold is an index of each period's mean monthly Pharmacare expenditures relative to the mean monthly Pharmacare expenditures in the period directly preceding the introduction of nitrates RP, April 1994 - October 1995.

		Pre-LCA Jan 93 - Mar 94	LCA Policy Apr 94 - Oct 95	RP of Nitrates Nov 95 - Jan 96	NTG Patch Exempted Feb 96 - Dec 96	RP of CCBs Jan 97 - May 99
NITRATES						
<i>Restricted</i>	NTG (SR)	69,514 116	59,677 100	12,867 22	19,934 33	12,264 21
	Pentaerythritol	307 133	231 100	44 19	59 26	44 19
	Iso. Mononitrate	0	4 100	83 2,075	101 2,525	123 3,075
	Iso. Mononitrate (SR)	0	18 100	65 361	73 406	102 567
	Iso. Dinitrate (SR)	695 146	477 100	75 16	107 22	46 10
<i>All Restricted Nitrates</i>		70,516 117	60,407 100	13,134 22	20,274 34	12,579 21
<i>Ref. Standard</i>	Iso. Dinitrate	3,472 261	1,332 100	3,258 245	2,487 187	1,811 136
	NTG Ointment	300 246	122 100	762 625	94 77	46 38
	<i>All Ref. Std. Nitrates</i>	3,772 259	1,454 100	4,020 276	2,581 178	1,857 128
<i>Variable</i>	NTG Patch	55,717 83	67,198 100	24,960 37	37,482 56	45,098 67
<i>Exempt</i>	NTG Sublingual	10,297 107	9,641 100	9,429 98	9,833 102	10,165 105
<i>All Nitrates</i>		140,302 101	138,700 100	51,543 37	70,170 51	69,699 50
CALCIUM CHANNEL BLOCKERS						
<i>Restricted</i>	Nifedipine	11,145 270	4,125 100	3,408 83	1,862 45	87 2
	Nifedipine (SR)	132,776 106	125,190 100	113,093 90	102,417 82	80,838 65
	Nicardipine	6,934 146	4,748 100	3,344 70	2,659 56	1,379 29
	Amlodipine	16,475 42	39,434 100	57,626 146	77,401 196	74,276 188
	<i>All Restricted CCBs</i>	167,330 96	173,497 100	177,471 102	184,339 106	156,580 90
<i>Ref. Standard</i>	Felodipine	14,805 64	22,972 100	26,464 115	27,216 118	50,084 218
<i>Exempt</i>	Diltiazem	49,379 226	21,865 100	16,092 74	12,698 58	7,654 35
	Diltiazem (SR)	211,758 101	208,989 100	194,134 93	193,063 92	127,317 61
	Verapamil	19,596 220	8,912 100	7,138 80	6,151 69	4,691 53
	Verapamil (SR)	47,783 96	49,594 100	49,945 101	47,098 95	31,785 64
	<i>All Exempt CCBs</i>	343,321 110	312,332 100	293,773 94	286,226 92	221,531 71
<i>All CCBs</i>		525,456 103	508,801 100	497,708 98	497,781 98	428,195 84
BETA BLOCKERS						
<i>Exempt</i>		154,651 112	138,550 100	136,750 99	132,902 96	143,565 104

Table 11 Mean patient-reimbursed drug expenditures per 100,000 senior Pharmacare beneficiaries per month, by cardiovascular drug type and policy period – nitrate drugs and substitutes

Highlighted in bold is an index of each period's mean monthly patient expenditures relative to the mean monthly patient expenditures in the period directly preceding the introduction of nitrates RP, April 1994 - October 1995.

		Pre-LCA	LCA Policy	RP of Nitrates	NTG Patch Exempted	RP of CCBs
		Jan 93 - Mar 94	Apr 94 - Oct 95	Nov 95 - Jan 96	Feb 96 - Dec 96	Jan 97 - May 99
NITRATES						
<i>Restricted</i>	NTG (SR)	0 0	227 100	7,456 3,285	3,944 1,737	2,080 916
	Pentaerythritol	0 0	2 100	66 3,300	31 1,550	15 750
	Iso. Mononitrate	0	21 100	247 1,176	191 910	145 690
	Iso. Mononitrate (SR)	0	69 100	143 207	125 181	114 165
	Iso. Dinitrate (SR)	0 0	2 100	81 4,050	13 650	10 500
<i>All Restricted Nitrates</i>		0 0	321 100	7,993 2,490	4,304 1,341	2,364 736
<i>Ref. Standard</i>	Iso. Dinitrate	0 0	47 100	199 423	105 223	89 189
	NTG Ointment	0 0	1 100	13 1,300	1 100	2 200
	<i>All Ref. Std. Nitrates</i>	0 0	48 100	212 442	106 221	91 190
<i>Variable</i>	NTG Patch	0 0	341 100	9,465 2,776	1,341 393	1,122 329
<i>Exempt</i>	NTG Sublingual	0 0	79 100	137 173	163 206	286 362
<i>All Nitrates</i>		0 0	789 100	17,807 2,257	5,914 750	3,863 490
CALCIUM CHANNEL BLOCKERS						
<i>Restricted</i>	Nifedipine	0 0	70 100	131 187	89 127	5 7
	Nifedipine (SR)	0 0	85 100	426 501	1,276 1,501	3,690 4,341
	Nicardipine	0 0	27 100	26 96	48 178	110 407
	Amlodipine	0 0	15 100	20 133	157 1,047	6,764 45,093
	<i>All Restricted CCBs</i>	0 0	197 100	603 306	1,570 797	10,569 5,365
<i>Ref. Standard</i>	Felodipine	0 0	90 100	310 344	489 543	843 937
<i>Exempt</i>	Diltiazem	0 0	172 100	352 205	285 166	255 148
	Diltiazem (SR)	0 0	1,124 100	2,652 236	2,261 201	3,636 323
	Verapamil	0 0	129 100	248 192	350 271	218 169
	Verapamil (SR)	0 0	254 100	726 286	777 306	1,184 466
	<i>All Exempt CCBs</i>	0 0	1,769 100	4,288 242	4,162 235	6,136 347
<i>All CCBs</i>		0 0	2,056 100	5,201 253	6,221 303	17,548 854
BETA BLOCKERS						
<i>Exempt</i>		0 0	923 100	2,447 265	3,258 353	4,311 467

Figure 10 Defined daily doses of ACE Inhibitor and CCB drugs dispensed per 100,000 seniors, by reimbursement status and month

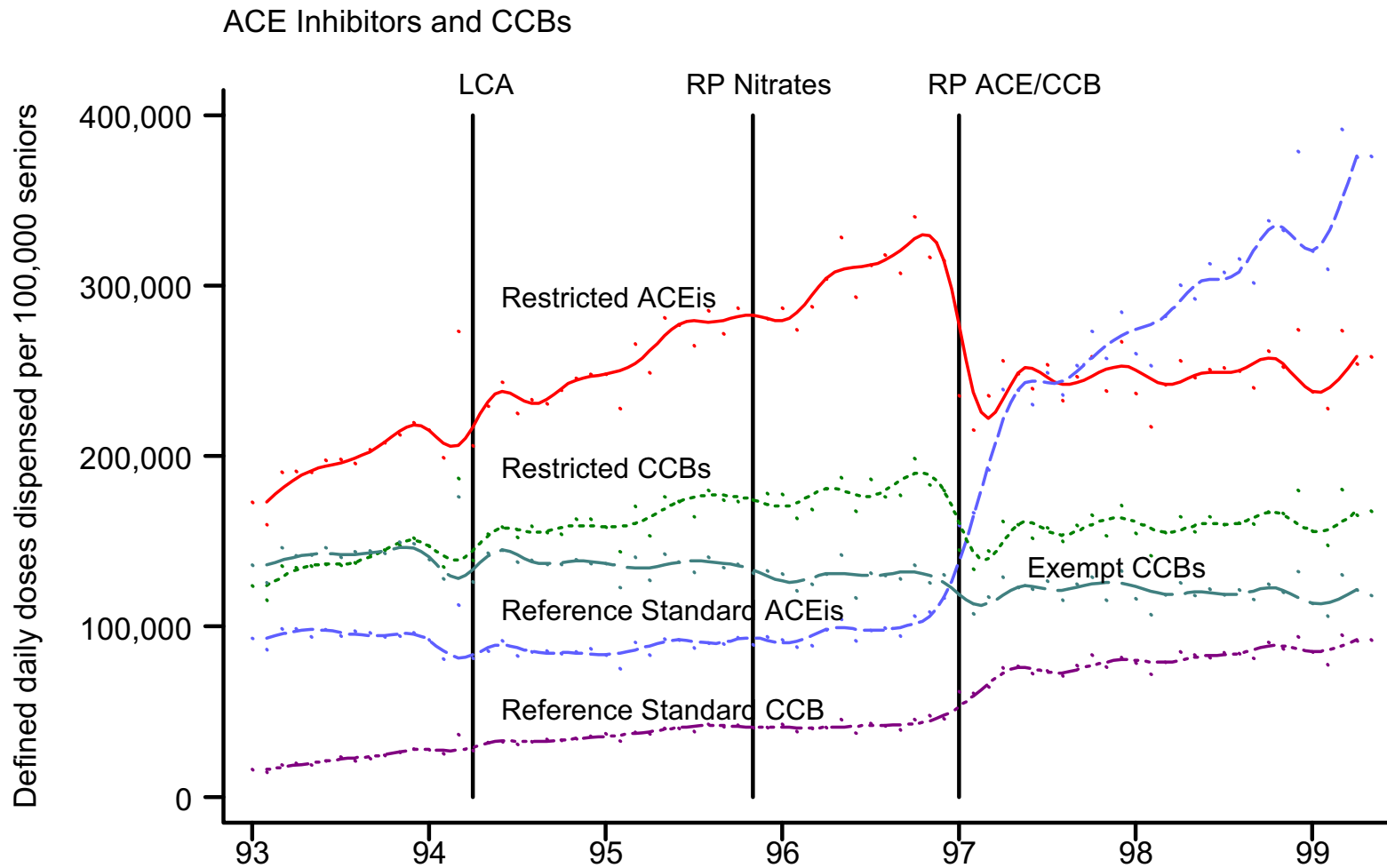


Figure 11 Defined daily doses of Substitute drugs dispensed per 100,000 seniors, by month

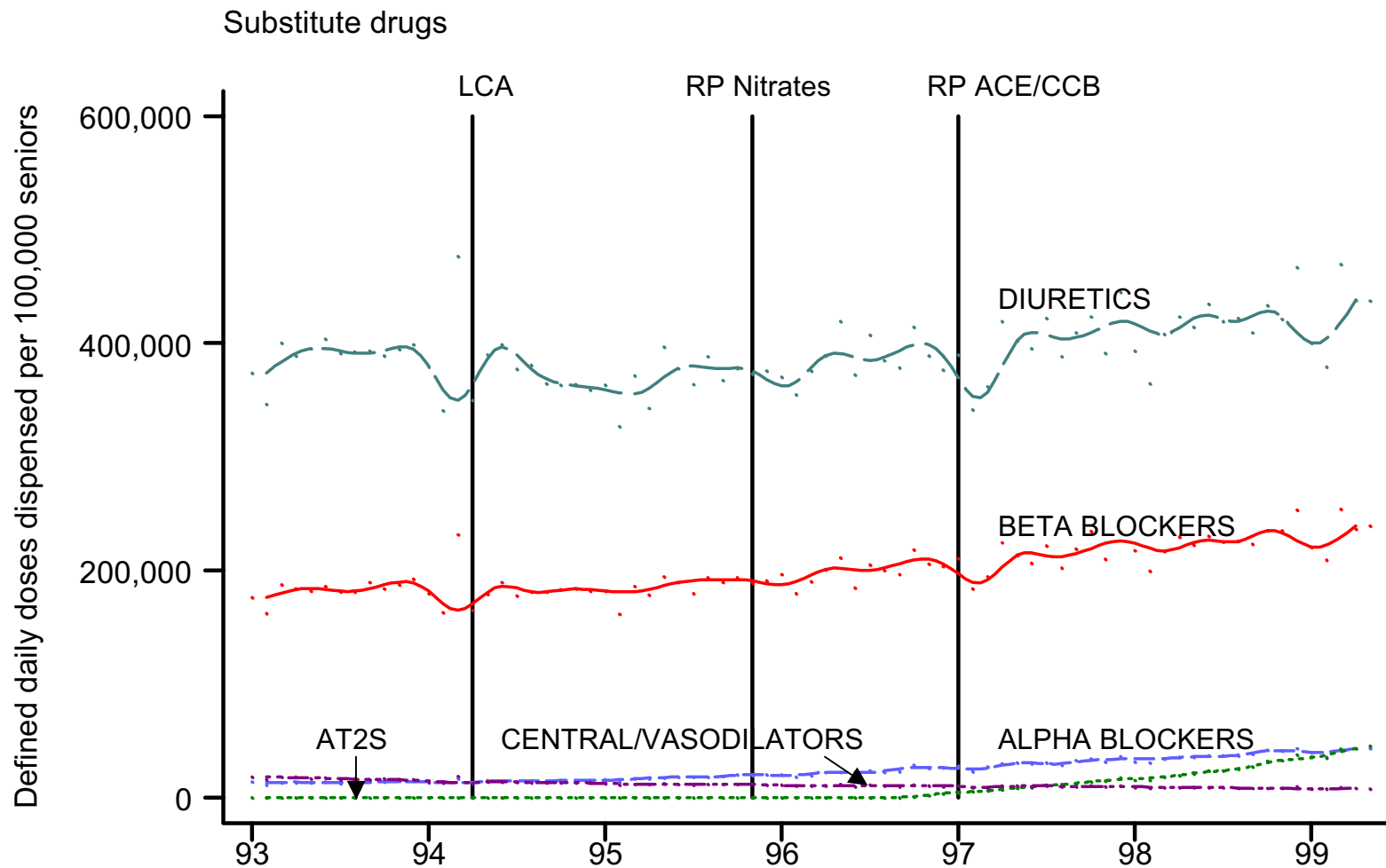


Figure 12 Pharmacare reimbursement per defined daily dose of ACE Inhibitor and CCB drugs, by reimbursement status and month

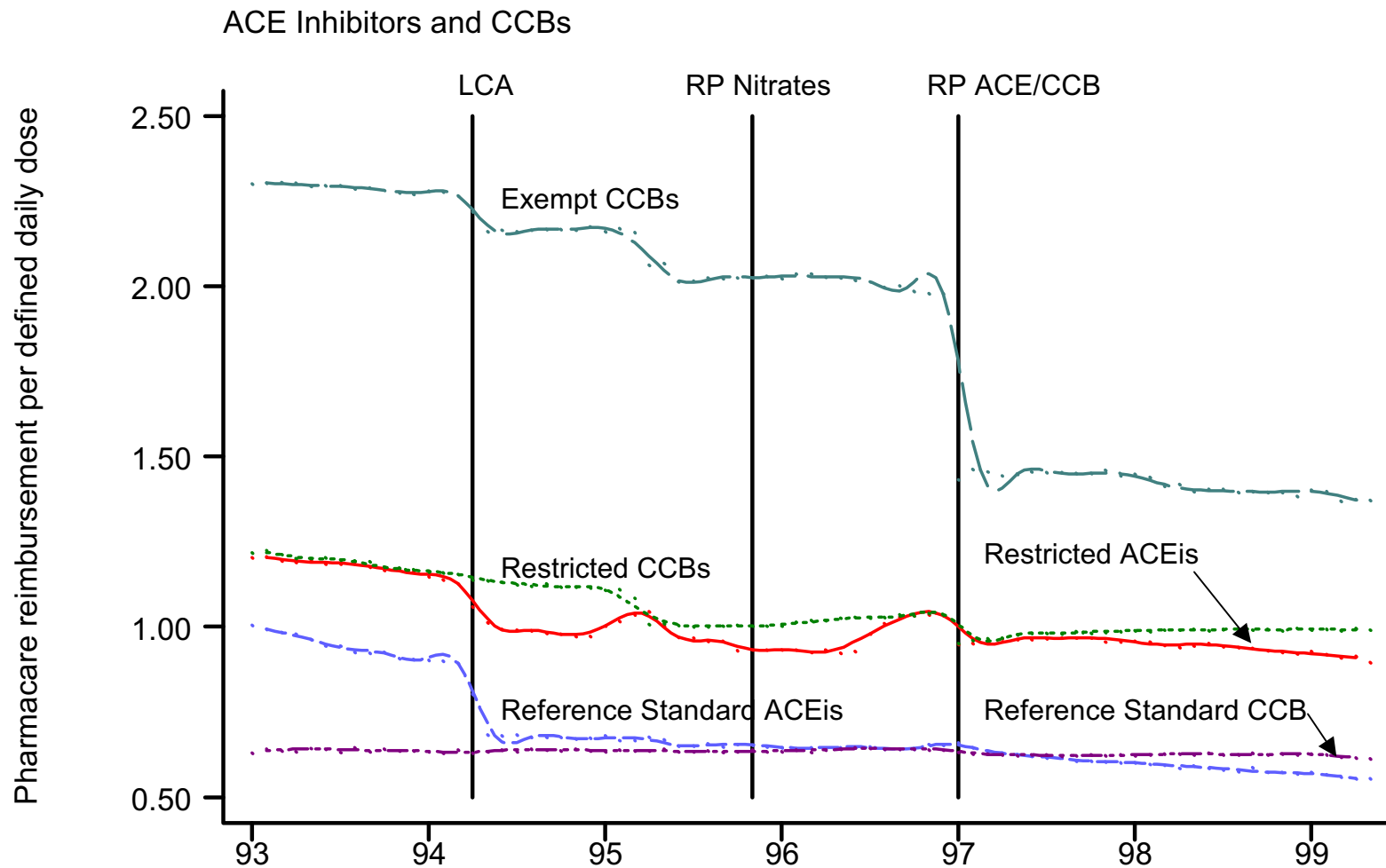


Figure 13 Pharmacare ingredient cost expenditures on ACE Inhibitor and CCB drugs dispensed per 100,000 seniors, by reimbursement status and month

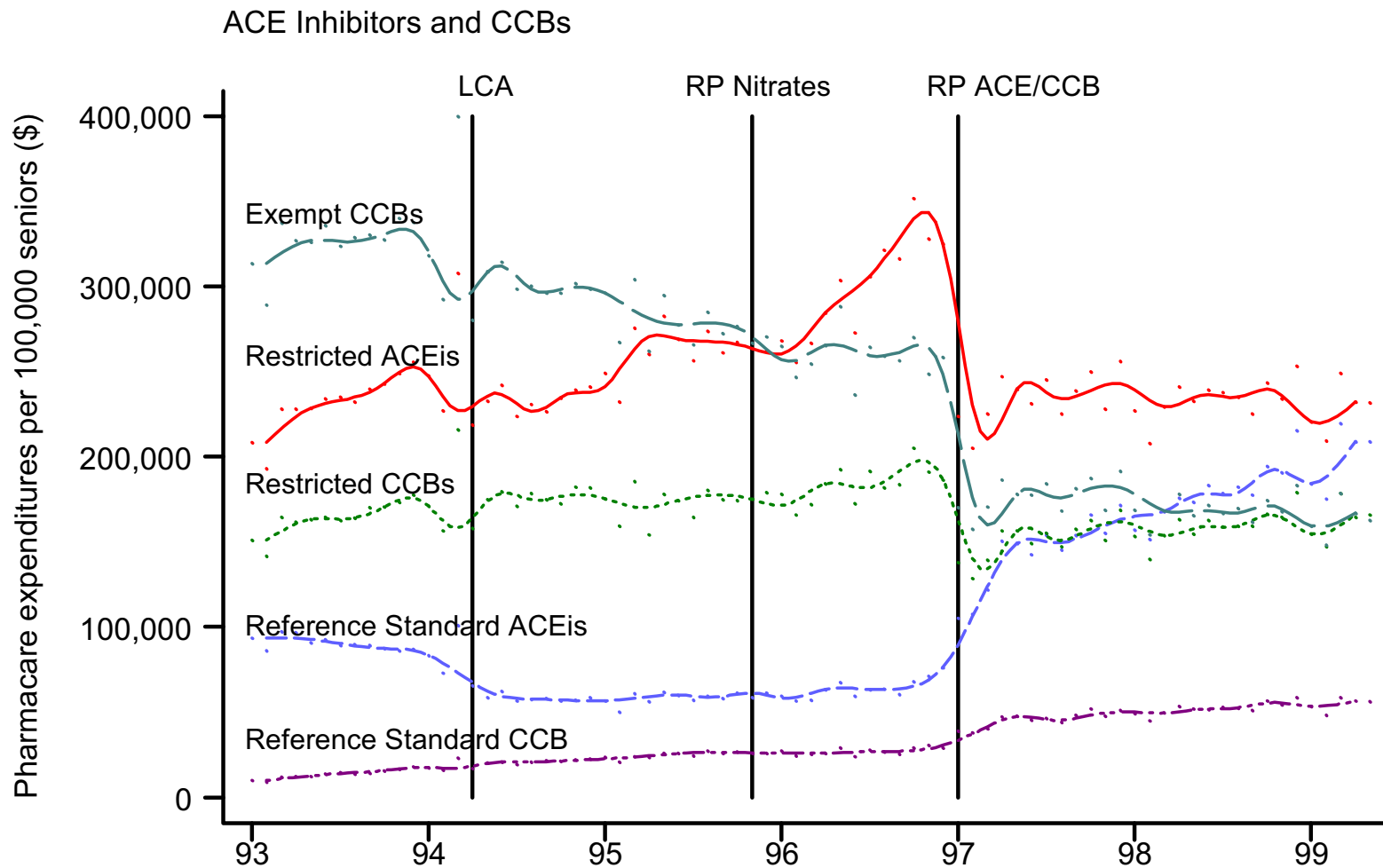


Figure 14 Pharmacare ingredient cost expenditures on Substitute drugs dispensed per 100,000 seniors, by month

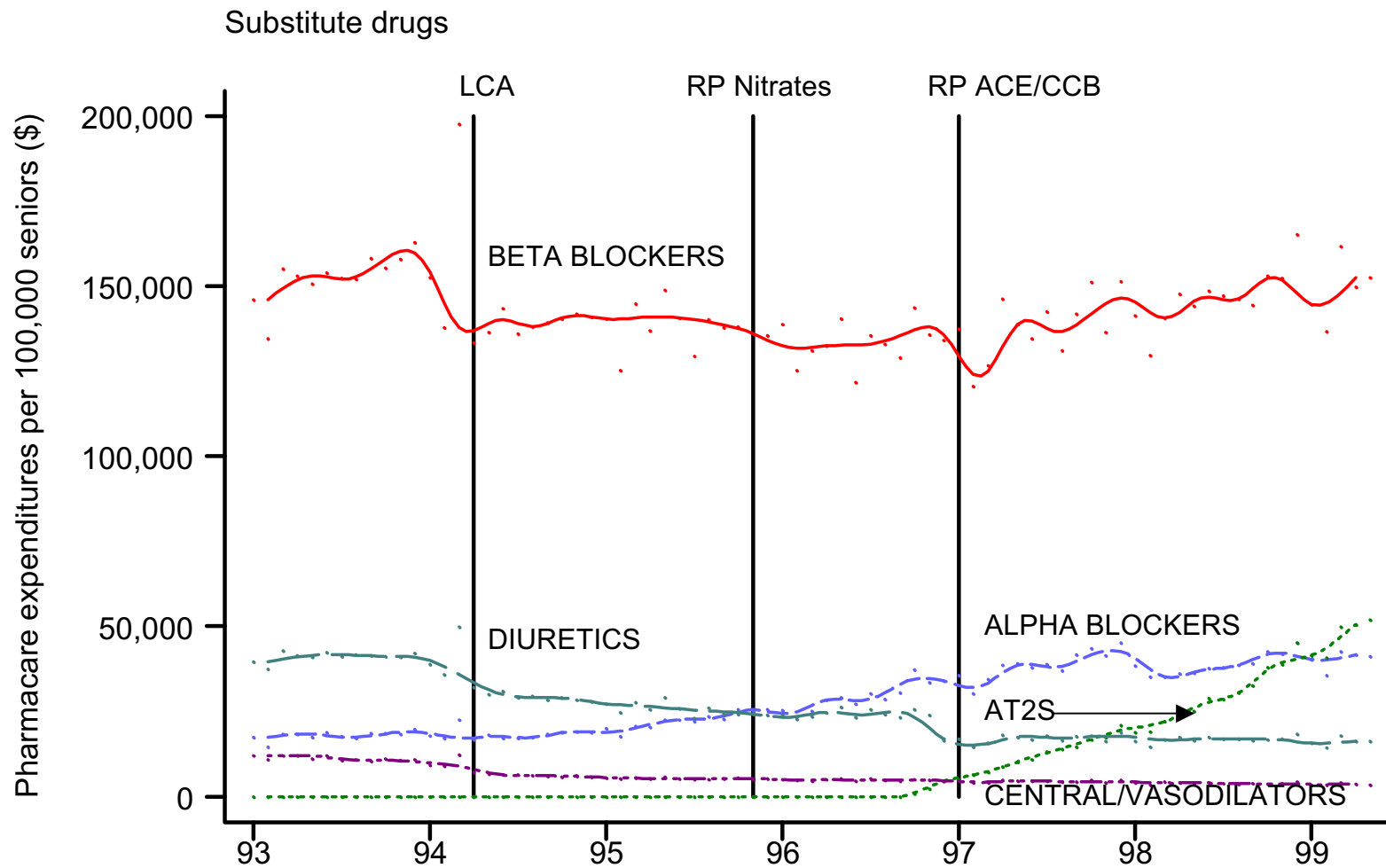


Figure 15 Patient ingredient cost expenditures on ACE Inhibitor and CCB drugs dispensed per 100,000 seniors, by reimbursement status and month

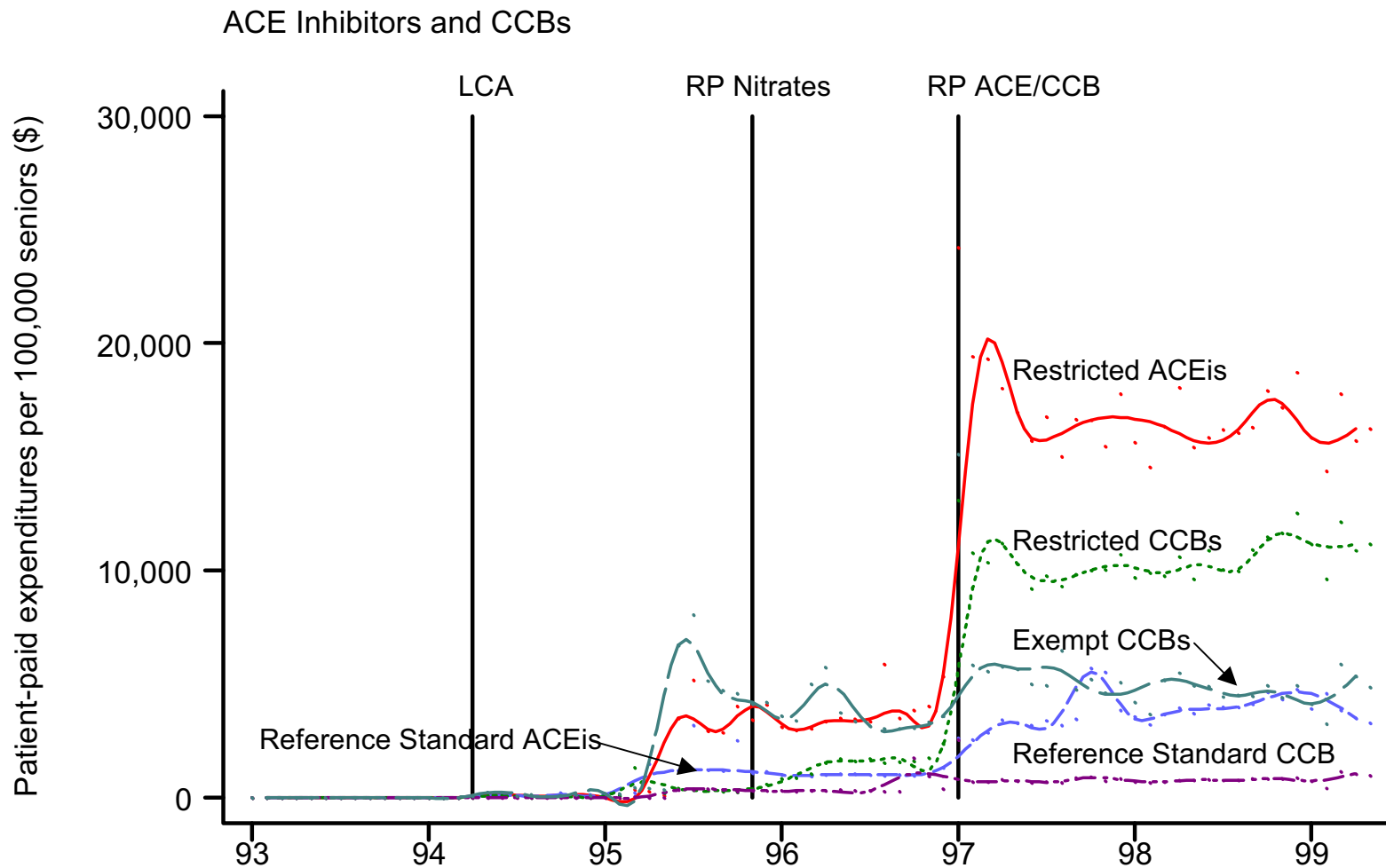


Figure 16 Actual and predicted Pharmacare expenditures on ACE inhibitors with and without RP, per 100,000 seniors, by month, with 95% confidence intervals

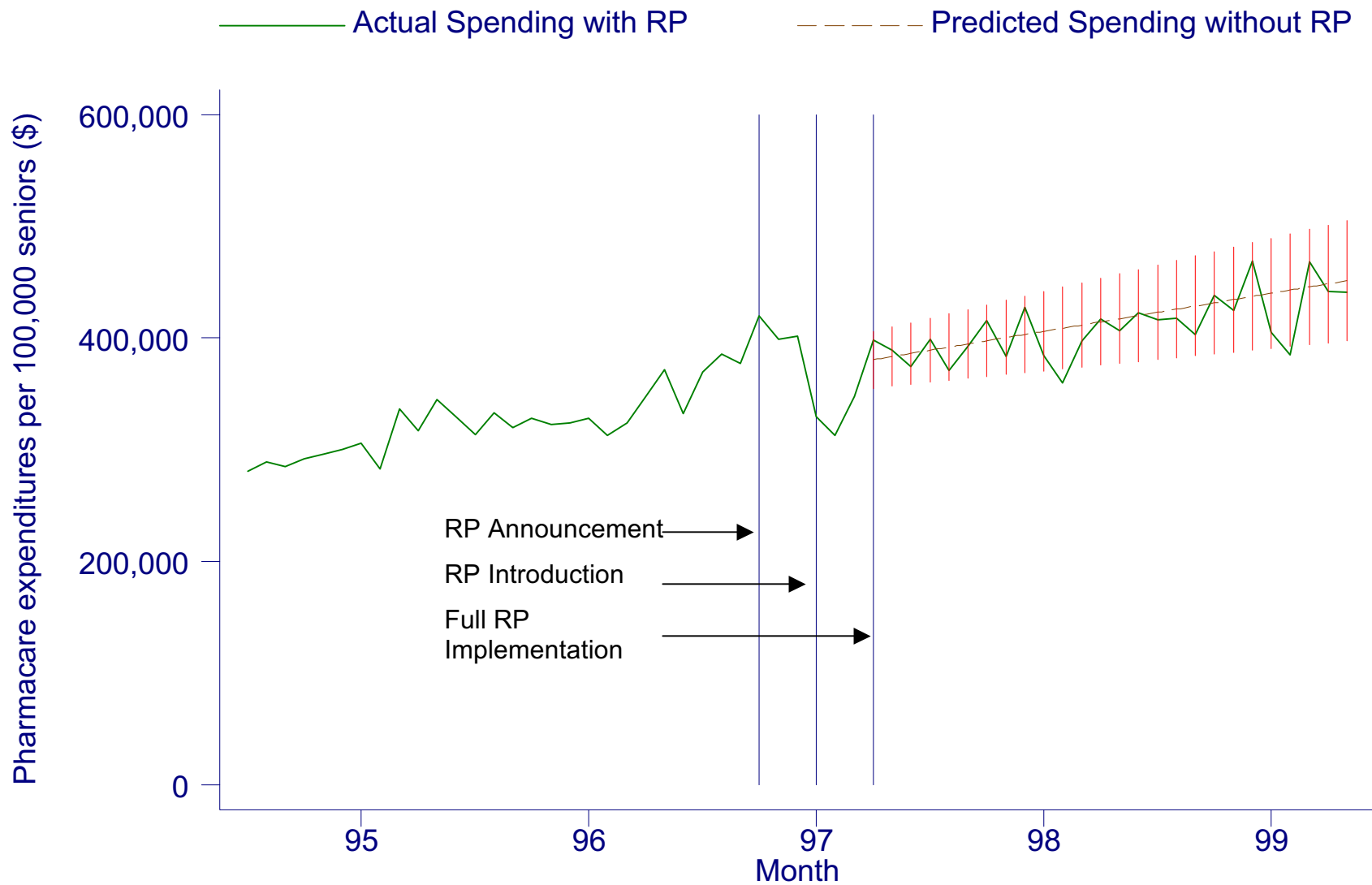


Figure 17 Actual and predicted Pharmacare expenditures on CCBs with and without RP, per 100,000 seniors, by month

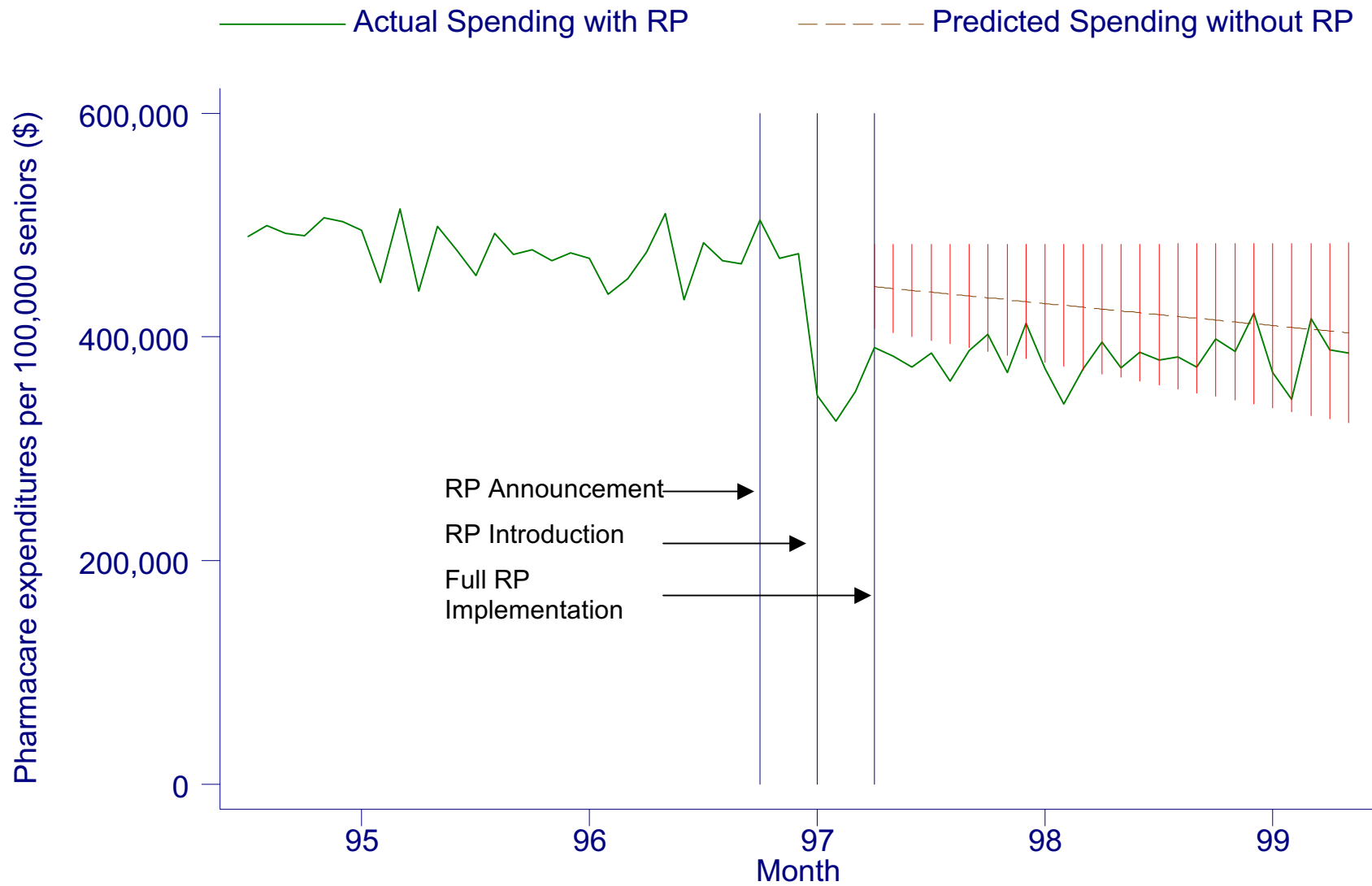


Table 12 Mean number of defined daily doses dispensed per 100,000 senior Pharmacare beneficiaries per month, by cardiovascular drug type and policy period – ACE inhibitor & CCB drugs and substitutes

Highlighted in bold is an index of each period's mean monthly DDDs dispensed relative to the mean monthly DDDs dispensed in the period directly preceding the announcement of the ACE inhibitor/CCB RP policy.

		Baseline Oct 95 - Sep 96	Announcement Oct 96 - Dec 96	Implementation Jan 97 - Mar 97	Post RP 1 Apr 97 - Mar 98	Post RP 2 Apr 98 - May 99
ACE INHIBITORS						
<i>Restricted</i>	Enalapril	181,600 100	194,570 107	128,003 70	130,799 72	126,312 70
	Lisinopril	81,095 100	89,599 110	67,482 83	74,227 92	78,610 97
	Fosinopril	15,348 100	17,836 116	14,044 92	16,629 108	19,211 125
	Cilazapril	13,265 100	15,769 119	14,841 112	18,104 136	23,548 178
	Benazepril	5,606 100	6,103 109	4,498 80	5,084 91	4,884 87
	<i>All Restricted ACEI</i>	296,914 100	323,877 109	228,868 77	244,843 82	252,565 85
<i>Ref. Std.</i>	Captopril	60,946 100	58,475 96	55,535 91	56,304 92	49,237 81
	Quinapril	11,412 100	18,345 161	45,707 401	70,529 618	94,129 825
	Ramipril	22,063 100	33,787 153	71,763 325	128,036 580	189,161 857
	<i>All Ref. Std. ACEI</i>	94,421 100	110,607 117	173,005 183	254,869 270	332,527 352
	<i>All ACE Inhibitors</i>	391,335 100	434,484 111	401,873 103	499,712 128	585,092 150
CALCIUM CHANNEL BLOCKERS						
<i>Restricted</i>	Nifedipine	3,811 100	1,649 43	171 4	167 4	101 3
	Nifedipine (SR)	115,976 100	112,207 97	90,550 78	94,215 81	89,843 77
	Nicardipine	1,276 100	987 77	804 63	706 55	553 43
	Amlodipine	55,059 100	72,469 132	49,622 90	61,888 112	73,661 134
	<i>All Restricted CCBs</i>	176,122 100	187,312 106	141,147 80	156,976 89	164,158 93
<i>Ref. Std.</i>	Felodipine	41,219 100	46,509 113	62,549 152	76,720 186	86,850 211
<i>Exempt</i>	Diltiazem	8,915 100	7,065 79	6,596 74	5,509 62	3,943 44
	Diltiazem (SR)	81,327 100	82,940 102	72,323 89	78,039 96	78,890 97
	Verapamil	7,347 100	6,711 91	6,257 85	5,914 80	4,921 67
	Verapamil (SR)	32,265 100	34,054 106	29,476 91	32,429 101	33,018 102
	<i>All Exempt CCBs</i>	129,854 100	130,770 101	114,652 88	121,891 94	120,772 93
	<i>All CCBs</i>	347,195 100	364,591 105	318,348 92	355,587 102	371,780 107
BETA BLOCKERS		194,950 100	209,269 107	196,308 101	216,587 111	231,426 119
ALPHA BLOCKERS		21,100 100	26,796 127	26,060 124	31,783 151	39,455 187
AT2S			2,140	5,119	12,809	31,721
CENTRAL/VASODILATORS		10,865 100	10,418 96	9,643 89	9,761 90	8,500 78
DIURETICS		381,486 100	393,230 103	364,400 96	405,065 106	426,318 112

Table 13 Mean Pharmacare reimbursement price per Defined Daily Dose, by cardiovascular drug type and policy period – ACE inhibitor & CCB drugs and substitutes

Highlighted in bold is an index of each period's mean monthly Pharmacare reimbursement per DDD relative to the mean monthly Pharmacare reimbursement per DDD in the period directly preceding the announcement of the ACE inhibitor/CCB RP policy.

		Time Period				
		Baseline	Announcement	Implementation	Post RP 1	Post RP 2
		Oct 95 - Sep 96	Oct 96 - Dec 96	Jan 97 - Mar 97	Apr 97 - Mar 98	Apr 98 - May 99
ACE INHIBITORS						
<i>Restricted</i>	Enalapril	1.07 100	1.22 114	1.13 106	1.16 109	1.14 107
	Lisinopril	0.77 100	0.76 99	0.73 95	0.74 96	0.73 95
	Fosinopril	1.06 100	1.05 99	1.01 95	1.01 96	0.99 94
	Cilazapril	0.56 100	0.55 98	0.52 92	0.52 92	0.51 91
	Benazepril	0.46 100	0.46 101	0.45 97	0.44 95	0.43 92
	<i>All Restricted ACEI</i>	0.95 100	1.03 109	0.95 100	0.96 101	0.93 98
<i>Ref. Std.</i>	Captopril	0.63 100	0.63 100	0.62 99	0.62 98	0.61 97
	Quinapril	0.99 100	1.02 103	1.01 102	0.97 98	0.92 93
	Ramipril	0.52 100	0.49 94	0.43 84	0.41 79	0.39 76
	<i>All Ref. Std. ACEI</i>	0.65 100	0.65 101	0.65 100	0.61 94	0.57 89
	<i>All ACE Inhibitors</i>	0.88 100	0.94 107	0.82 94	0.78 89	0.73 83
CALCIUM CHANNEL BLOCKERS						
<i>Restricted</i>	Nifedipine	0.68 100	0.67 99	0.64 95	0.66 97	0.62 92
	Nifedipine (SR)	0.92 100	0.91 99	0.88 96	0.88 96	0.88 96
	Nicardipine	2.35 100	2.31 98	2.05 87	2.15 92	2.17 92
	Amlodipine	1.23 100	1.23 100	1.10 89	1.12 92	1.12 91
	<i>All Restricted CCBs</i>	1.02 100	1.04 102	0.96 94	0.98 97	0.99 97
<i>Ref. Std.</i>	Felodipine	0.64 100	0.64 100	0.63 98	0.62 98	0.62 98
<i>Exempt</i>	Diltiazem	1.60 100	1.60 100	1.58 99	1.57 99	1.57 98
	Diltiazem (SR)	2.37 100	2.37 100	1.68 71	1.68 71	1.59 67
	Verapamil	0.89 100	0.88 98	0.87 97	0.86 96	0.85 95
	Verapamil (SR)	1.51 100	1.33 88	0.97 65	0.98 65	0.98 65
	<i>All Exempt CCBs</i>	2.02 100	1.98 98	1.45 72	1.45 72	1.39 69
	<i>All CCBs</i>	1.35 100	1.33 98	1.07 79	1.06 79	1.04 77
BETA BLOCKERS		0.68 100	0.66 97	0.65 96	0.65 95	0.65 95
ALPHA BLOCKERS		1.28 100	1.31 102	1.29 100	1.24 97	1.01 79
AT2S		-	1.24 -	1.22 -	1.22 -	1.19 -
CENTRAL/VASODILATORS		0.46 100	0.47 101	0.46 99	0.46 99	0.46 98
DIURETICS		0.06 100	0.06 88	0.04 69	0.04 67	0.04 62

Table 14 Mean Pharmacare-reimbursed drug expenditures per 100,000 senior Pharmacare beneficiaries per month, by cardiovascular drug type and policy period – ACE inhibitor & CCB drugs and substitutes

Highlighted in bold is an index of each period's mean monthly Pharmacare reimbursement per DDD relative to the mean monthly Pharmacare reimbursement per DDD in the period directly preceding the announcement of the ACE inhibitor/CCB RP policy.

		Baseline Oct 95 - Sep 96	Announcement Oct 96 - Dec 96	Implementation Jan 97 - Mar 97	Post RP 1 Apr 97 - Mar 98	Post RP 2 Apr 98 - May 99
ACE INHIBITORS						
<i>Restricted</i>	Enalapril	193,916 100	236,519 122	145,075 75	152,284 79	144,237 74
	Lisinopril	62,197 100	68,172 110	49,171 79	54,856 88	57,320 92
	Fosinopril	16,193 100	18,718 116	14,141 87	16,812 104	19,009 117
	Cilazapril	7,454 100	8,710 117	7,673 103	9,340 125	12,007 161
	Benazepril	2,585 100	2,832 110	2,013 78	2,229 86	2,078 80
	<i>All Restricted ACEI</i>	282,345 100	334,951 119	218,073 77	235,521 83	234,651 83
<i>Ref. Std.</i>	Captopril	38,397 100	36,707 96	34,659 90	34,865 91	30,126 78
	Quinapril	11,295 100	18,765 166	46,119 408	68,379 605	86,428 765
	Ramipril	11,433 100	16,526 145	31,118 272	52,199 457	74,136 648
	<i>All Ref. Std. ACEI</i>	61,125 100	71,998 118	111,896 183	155,443 254	190,690 312
<i>All ACE Inhibitors</i>		343,470 100	406,949 118	329,969 96	390,964 114	425,341 124
CALCIUM CHANNEL BLOCKERS						
<i>Restricted</i>	Nifedipine	2,574 100	1,105 43	110 4	109 4	63 2
	Nifedipine (SR)	106,234 100	101,735 96	79,346 75	83,187 78	79,145 75
	Nicardipine	2,997 100	2,278 76	1,648 55	1,520 51	1,200 40
	Amlodipine	67,522 100	89,117 132	54,434 81	69,593 103	82,542 122
	<i>All Restricted CCBs</i>	179,327 100	194,235 108	135,538 76	154,409 86	162,950 91
<i>Ref. Std.</i>	Felodipine	26,352 100	29,817 113	39,362 149	47,926 182	54,232 206
<i>Exempt</i>	Diltiazem	14,249 100	11,307 79	10,428 73	8,673 61	6,187 43
	Diltiazem (SR)	193,095 100	196,461 102	121,745 63	130,834 68	125,497 65
	Verapamil	6,567 100	5,884 90	5,420 83	5,090 78	4,193 64
	Verapamil (SR)	48,637 100	45,414 93	28,659 59	31,779 65	32,459 67
	<i>All Exempt CCBs</i>	262,548 100	259,066 99	166,252 63	176,376 67	168,336 64
<i>All CCBs</i>		468,227 100	483,118 103	341,152 73	378,711 81	385,518 82
BETA BLOCKERS		133,054 100	137,827 104	128,118 96	140,449 106	149,546 112
ALPHA BLOCKERS		27,033 100	34,979 129	33,534 124	39,401 146	39,788 147
AT2S			2,648	6,236	15,582	37,624
CENTRAL/VASODILATORS		5,030 100	4,882 97	4,409 88	4,456 89	3,874 77
DIURETICS		24,195 100	22,047 91	15,841 65	17,120 71	16,792 69

Table 15 Mean patient-reimbursed drug expenditures per 100,000 senior Pharmacare beneficiaries per month, by cardiovascular drug type and policy period – ACE inhibitor & CCB drugs and substitutes

Highlighted in bold is an index of each period's mean monthly patient expenditures relative to the mean monthly patient expenditures in the period directly preceding the announcement of the ACE inhibitor/CCB RP policy.

		Baseline Oct 95 - Sep 96	Announcement Oct 96 - Dec 96	Implementation Jan 97 - Mar 97	Post RP 1 Apr 97 - Mar 98	Post RP 2 Apr 98 - May 99
ACE INHIBITORS						
<i>Restricted</i>	Enalapril	2,628 100	3,179 121	15,922 606	11,630 443	11,411 434
	Lisinopril	710 100	872 123	3,398 479	3,044 429	3,188 449
	Fosinopril	175 100	206 118	1,097 627	995 569	1,143 653
	Cilazapril	93 100	109 117	473 509	500 538	662 712
	Benazepril	29 100	32 110	95 328	122 421	138 476
	<i>All Restricted ACEI</i>	3,635 100	4,398 121	20,985 577	16,291 448	16,542 455
<i>Ref. Std.</i>	Captopril	791 100	611 77	666 84	688 87	641 81
	Quinapril	166 100	274 165	1,197 721	1,715 1033	1,818 1095
	Ramipril	183 100	225 123	821 449	1,383 756	1,589 868
	<i>All Ref. Std. ACEI</i>	1,140 100	1,110 97	2,684 235	3,786 332	4,048 355
	<i>All ACE Inhibitors</i>	4,775 100	5,508 115	23,669 496	20,077 420	20,590 431
CALCIUM CHANNEL BLOCKERS						
<i>Restricted</i>	Nifedipine	113 100	42 37	4 4	8 7	2 2
	Nifedipine (SR)	916 100	1,463 160	4,369 477	3,707 405	3,531 385
	Nicardipine	45 100	43 96	235 522	118 262	75 167
	Amlodipine	61 100	356 584	6,791 11133	6,140 10066	7,293 11956
	<i>All Restricted CCBs</i>	1,135 100	1,904 168	11,399 1004	9,973 879	10,901 960
<i>Ref. Std.</i>	Felodipine	296 100	1,012 342	1,318 445	746 252	824 278
<i>Exempt</i>	Diltiazem	320 100	271 85	309 97	284 89	219 68
	Diltiazem (SR)	2,418 100	2,267 94	6,351 263	3,314 137	3,330 138
	Verapamil	345 100	249 72	259 75	330 96	112 32
	Verapamil (SR)	826 100	542 66	1,921 233	1,116 135	1,084 131
	<i>All Exempt CCBs</i>	3,909 100	3,329 85	8,840 226	5,044 129	4,745 121
	<i>All CCBs</i>	5,340 100	6,245 117	21,557 404	15,763 295	16,470 308
BETA BLOCKERS		3,091 100	2,934 95	3,483 113	4,359 141	4,447 144
ALPHA BLOCKERS		412 100	503 122	735 178	966 234	1,016 247
AT2S			0	59	278	563
CENTRAL/VASODILATORS		204 100	206 101	185 91	193 95	193 95
DIURETICS		1,213 100	813 67	753 62	836 69	1,519 125

4.2 Patient level analyses

4.2.1 Sample selection

We first identified those subjects who were using either Restricted or Unrestricted drugs in the 19 of the 20 weeks before the introduction of RP. This yielded 13,128 nitrates users, 35,944 ACE inhibitor (but not CCB) users, 34,566 CCB (but not ACE inhibitor) users, and 7,090 users of both ACE inhibitor and CCB drugs. A large proportion of the latter group (86% or 6,094 subjects) took either a Restricted ACE inhibitor or CCB, with 2,385 (34%) taking both these types of drugs. The effects of RP on the outcomes of these individuals will be investigated in future research.

Of the 13,128 nitrate users, 953 (7%) went on to use a Restricted ACE inhibitor (n=556) or a Restricted CCB (n=109) or both a Restricted ACE inhibitor and CCB (n=288) prior to the introduction of RP of these drugs in January 1997. We do not focus directly on the effects of the introduction of the RP as applied to ACE inhibitors & CCBs on nitrate users given that one would expect that they would be distributed evenly between exposed and comparator groups.

A total of 213 nitrates users (1.6%), 60 ACE inhibitor users (0.2%) and 138 CCB users (0.4%) were excluded from subsequent analyses because these individuals were using both restricted and unrestricted drugs pre-RP and their primary drug could not be ascertained. Of the remaining subjects, 14% of nitrates users, 20% of ACE inhibitor users and 58% of CCB users were using an unrestricted drug continuously before the introduction of RP (Table 16). The remaining subjects were using a Restricted drug pre-RP, and they represent those who were potentially exposed to RP. Of those potentially exposed, the rates of patient exemption (defined as having received an exemption for all Restricted drugs dispensed post-RP) varied considerably by drug group: only 16% of the 11,155 subjects taking restricted nitrates pre-policy received exemptions, compared to 49% of the 28,564 restricted ACE inhibitor users and 57% of the 14,342 restricted CCB users. Conversely, the percentage of restricted drug users who neither paid out of pocket nor received exemptions was highest for restricted nitrate users (62%), followed by 24% of restricted ACE inhibitor users and 20% of restricted CCB users. Tables of descriptive statistics of the pre-RP characteristics (including demographics and health care use) of nitrates, ACE inhibitor and CCB users, by RP exposure status, are found in Appendix 2.

Table 16 Distribution of subjects assigned in exposed and comparator groups, by drug group

Exposure / comparator group	Nitrates		ACE inhibitors		CCBs	
	Frequency	Percent	Frequency	Percent	Frequency	Percent
<i>Exempt:</i> Restricted drug user pre-RP, Exempted thereafter	1,812	14.0	13,861	38.6	8,226	23.9

	Nitrates		ACE inhibitors		CCBs	
<i>Paid</i> : Restricted drug user pre-RP, Paid and/or Paid & Exempted thereafter	2,467	19.1	7,951	22.2	3,268	9.5
<i>Neither</i> : Restricted drug user pre-RP, neither Paid nor Exempted thereafter	6,876	53.2	6,752	18.8	2,848	8.3
Unrestricted drug user pre-RP	1,760	13.6	7,320	20.4	20,086	58.3
Total	12,915	100.0	35,884	100.0	34,428	100.0

Note: the first 3 groups constitute the exposed group – those who used Restricted drugs pre-RP. We measure exemption from RP by examining the reimbursement status of Restricted drugs dispensed post-RP. Exemptees received exemptions for all Restricted drugs dispensed post-RP. These individuals could still have been affected by RP however. For example, they could have switched to an Unrestricted drug and then switched back

4.2.2 Switching behaviour

Rates of switching from Restricted drugs to Unrestricted drugs or substitutes varied by drug class (Tables 17-19 and Figures 18-20). Among Restricted nitrate users, 34% of subjects switched post-RP (until the end of the sample follow up period March 1998); the figures for ACE inhibitor users and CCB users were 25% and 21%, respectively. One reason for the differences in switching rates between nitrates and the other drug groups is that the followup period is 14 months longer for nitrates. Some switching also occurred among those who were using Unrestricted drugs prior to the introduction of RP, suggesting that some of these subjects actually used Restricted drugs following RP. The rate of switching in these groups was low however.

Table 17 Frequency and percentage of Nitrate users who switch to an Unrestricted Nitrate, or substitute after the introduction of RP, by Nitrates RP exposure status.

Nitrates RP exposure status:	Non-switchers: frequency, row %, and column %	Switchers: frequency, row %, and column %	Totals: frequency, row %, and column %
Restricted	7,323 65.65 80.88	3,832 34.35 99.25	11,155 100.00 86.37
Unrestricted	1,731 98.35 19.12	29 1.65 0.75	1,760 100 13.63
Total	9,054 70.10 100	3,861 29.90 100	12,915 100 100

Table 18 Frequency and percentage of ACE inhibitor users who switch to an Unrestricted ACE inhibitor, or substitute after the introduction of RP, by ACE inhibitor RP exposure status.

ACE inhibitors RP exposure status:	Non-switchers: frequency, row %, and column %	Switchers: frequency, row %, and column %	Totals: frequency, row %, and column %
Restricted	21,407 74.94 74.66	7,157 25.06 99.26	28,564 100.00 79.60
Unrestricted	7,267 99.28 25.34	53 0.72 0.74	7,320 100 20.40
Total	28,674 79.91 100	7,210 20.09 100	35,884 100 100

Table 19 Frequency and percentage of CCB users who switch to an Unrestricted CCB, or substitute after the introduction of RP, by CCB RP exposure status.

CCBs RP exposure status:	Non-switchers: frequency, row %, and column %	Switchers: frequency, row %, and column %	Totals: frequency, row %, and column %
Restricted	11,355 79.17 36.33	2,987 20.83 94.02	14,342 100.00 41.66
Unrestricted	19,896 99.05 63.67	190 0.95 5.98	20,086 100 58.34
Total	31,251 90.77 100	3,177 9.23 100	34,428 100 100

Figure 18 Percentage of nitrates users who switch from a Restricted drug to an Unrestricted drug or substitute, by week. (RP introduction date identified in figure)

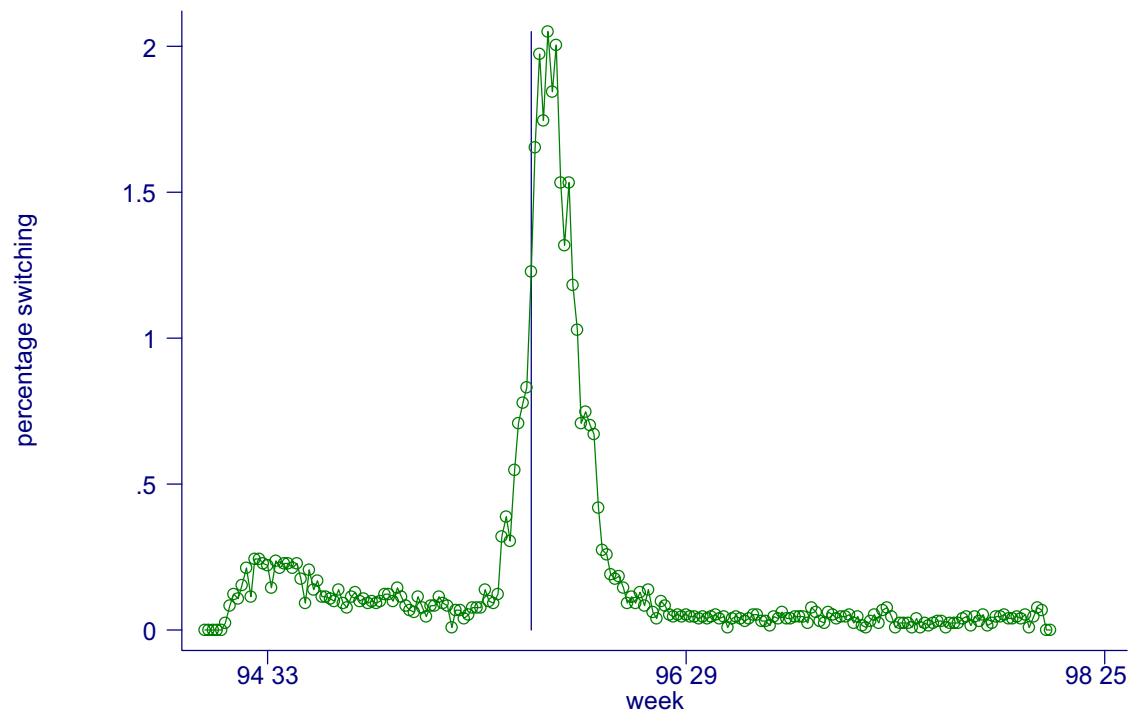


Figure 19 Percentage of ACE inhibitor users who switch from a Restricted drug to an Unrestricted drug or substitute, by week. (RP introduction date identified in figure)

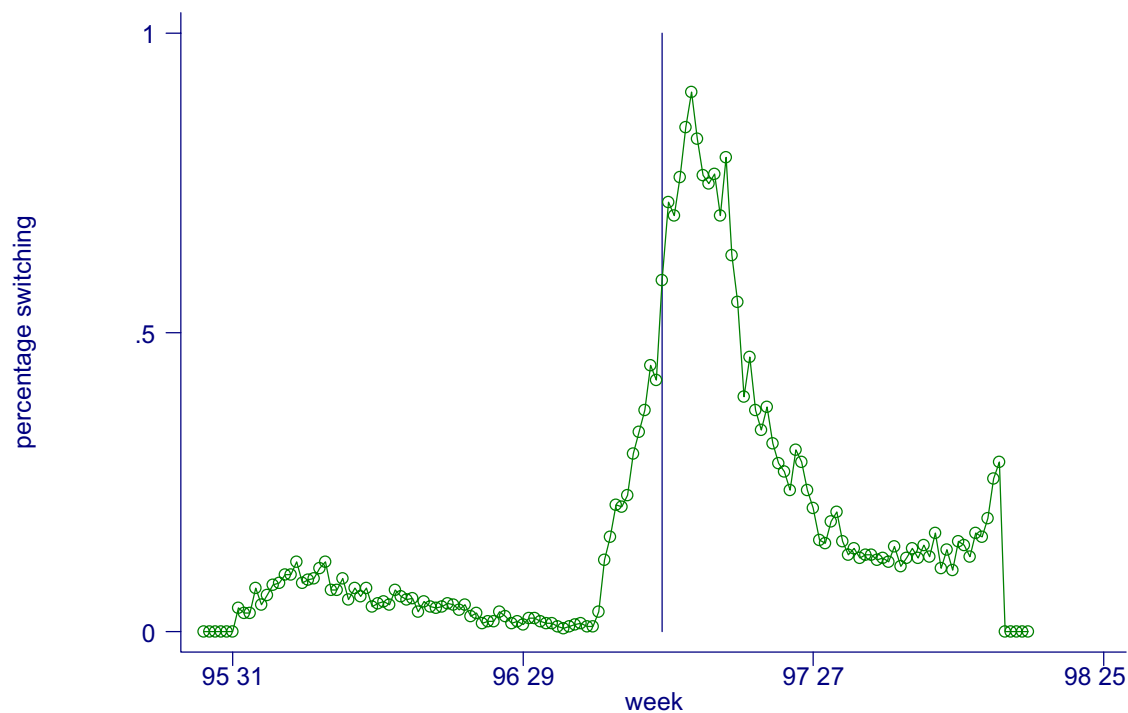
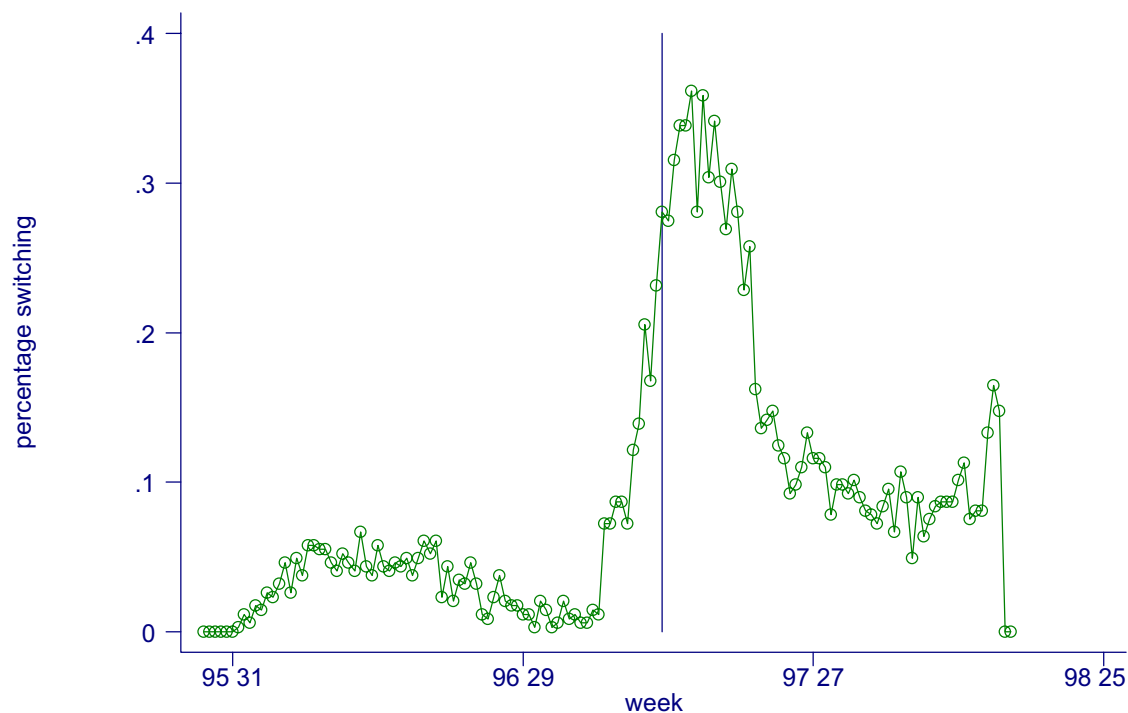


Figure 20 Percentage of CCB users who switch from a Restricted drug to an Unrestricted drug or substitute, by week. (RP introduction date identified in figure)



The appropriateness of using subjects who consumed Unrestricted drugs pre-RP as comparators to those who consumed Restricted drugs pre-RP depends on the extent that Unrestricted users were not constrained by the additional charges for Restricted drugs. To test this we estimated rates at which Unrestricted drug users switched to Restricted drugs when RP was not yet introduced. We first identified those who consumed Unrestricted drugs at least 19 of the 20 weeks in the period ending 1 year *prior* to the announcement of RP. We then determined their rates of switching to Restricted drugs over the year ending with the actual announcement of RP. We used the same generous definition of switching that was used earlier – a switch was said to have occurred if an individual started using a Restricted drug within ± 15 weeks of having stopped taking an Unrestricted drug. The 1 year switching rates were low: 3.9% of the 2,032 Unrestricted nitrate users, 4.0% of the 7,034 Unrestricted ACE inhibitor users and 1.9% of the CCB users switched. Nevertheless, it is apparent from Tables 20, 22, and 24 that a small minority of pre-RP Unrestricted drug users were using Restricted drugs post-policy and it would be preferable to remove all such individuals from the group of comparators. This will be accomplished in future research.

Table 20 Cross tabulation of types of nitrate drugs used before and after the introduction of nitrates RP. Subsample of those taking restricted nitrates pre-RP.

Pre RP	Post RP								
	000	001	010	011	100	101	110	111	Total
000	164	87	95	18	90	7	7	0	468
	35.0	18.6	20.3	3.9	19.2	1.5	1.5	0.0	100.0
	7.0	3.8	4.4	6.5	2.6	2.6	2.4	0.0	4.2
001	1	3	1	0	2	0	0	0	7
	14.3	42.9	14.3	0.0	28.6	0.0	0.0	0.0	100.0
	0.0	0.1	0.1	0.0	0.1	0.0	0.0	0.0	0.1
010	1,217	1,948	2,020	251	308	102	129	15	5,990
	20.3	32.5	33.7	4.2	5.1	1.7	2.2	0.3	100.0
	52.2	84.0	92.4	90.6	8.9	38.1	44.0	51.7	53.7
011	3	8	7	0	0	0	1	0	19
	15.8	42.1	36.8	0.0	0.0	0.0	5.3	0.0	100.0
	0.1	0.3	0.3	0.0	0.0	0.0	0.3	0.0	0.2
100	850	216	11	2	2,947	86	16	0	4,128
	20.6	5.2	0.3	0.1	71.4	2.1	0.4	0.0	100.0
	36.5	9.3	0.5	0.7	85.4	32.1	5.5	0.0	37.0
101	6	2	1	0	15	7	1	0	32
	18.8	6.3	3.1	0.0	46.9	21.9	3.1	0.0	100.0
	0.3	0.1	0.1	0.0	0.4	2.6	0.3	0.0	0.3
110	89	55	51	6	91	65	138	14	509
	17.5	10.8	10.0	1.2	17.9	12.8	27.1	2.8	100.0
	3.8	2.4	2.3	2.2	2.6	24.3	47.1	48.3	4.6
111	0	0	0	0	0	1	1	0	2
	0.0	0.0	0.0	0.0	0.0	50.0	50.0	0.0	100.0
	0.0	0.0	0.0	0.0	0.0	0.4	0.3	0.0	0.0
Total	2,330	2,319	2,186	277	3,453	268	293	29	11,155
	20.9	20.8	19.6	2.5	31.0	2.4	2.6	0.3	100.0
	100.0	100.0	100.0	100.0	100.0	100.0	100.0	100.0	100.0

Notes:

The first digit indicates the use of the NTG Patch (=1), or not (=0), the second indicates the use of another Restricted nitrate, and the third digit indicates use of an Unrestricted nitrate.

Period of pre-RP use: 114 day period ending September 16, 1995; Period of post-RP use: 114 day period beginning February 1, 1996 (at which point in time the reimbursement of 0.2 and 0.4 mg patch was no longer restricted under the RP policy).

The first entry in each cell is the frequency, the second entry is the row percentage and the third entry, the column percentage.

Table 21 Cross tabulation of types of nitrate drugs used before and after the introduction of nitrates RP. Subsample of those taking unrestricted nitrates pre-RP.

Pre RP	Post RP							Total
	000	001	010	011	100	101	110	
000	36	82	1	0	4	1	0	124
	29.0	66.1	0.8	0.0	3.2	0.8	0.0	100.0
	12.2	6.1	50.0	0.0	8.2	1.6	0.0	7.1
001	245	1,239	0	1	31	34	1	1,551
	15.8	79.9	0.0	0.1	2.0	2.2	0.1	100.0
	83.3	91.8	0.0	50.0	63.3	54.8	100.0	88.1
010	0	1	1	0	0	0	0	2
	0.0	50.0	50.0	0.0	0.0	0.0	0.0	100.0
	0.0	0.1	50.0	0.0	0.0	0.0	0.0	0.1
011	0	5	0	1	0	0	0	6
	0.0	83.3	0.0	16.7	0.0	0.0	0.0	100.0
	0.0	0.4	0.0	50.0	0.0	0.0	0.0	0.3
100	5	3	0	0	5	3	0	16
	31.3	18.8	0.0	0.0	31.3	18.8	0.0	100.0
	1.7	0.2	0.0	0.0	10.2	4.8	0.0	0.9
101	8	20	0	0	9	24	0	61
	13.1	32.8	0.0	0.0	14.8	39.3	0.0	100.0
	2.7	1.5	0.0	0.0	18.4	38.7	0.0	3.5
Total	294	1,350	2	2	49	62	1	1,760
	16.7	76.7	0.1	0.1	2.8	3.5	0.1	100.0
	100.0	100.0	100.0	100.0	100.0	100.0	100.0	100.0

Notes:

The first digit indicates the use of the NTG Patch (=1), or not (=0), the second indicates the use of another Restricted nitrate, and the third digit indicates use of an Unrestricted nitrate.

Period of pre-RP use: 114 day period ending September 16, 1995; Period of post-RP use: 114 day period beginning February 1, 1996 (at which point in time the reimbursement of 0.2 and 0.4 mg patch was no longer restricted under the RP policy).

The first entry in each cell is the frequency, the second entry is the row percentage and the third entry, the column percentage.

Table 22 Cross tabulation of ACE inhibitor and substitute drug use before and after RP, by RP reimbursement status. Subsample of those taking restricted ACE inhibitors pre-RP.

Pre RP	Post RP								Total
	000	001	010	011	100	101	110	111	
000	163	59	86	71	377	194	12	16	978
	16.7	6.0	8.8	7.3	38.6	19.8	1.2	1.6	100.0
	6.5	3.9	4.6	2.7	4.2	2.0	4.1	2.0	3.4
001	34	51	6	60	27	212	1	9	400
	8.5	12.8	1.5	15.0	6.8	53.0	0.3	2.3	100.0
	1.4	3.4	0.3	2.3	0.3	2.1	0.3	1.1	1.4
010	1	1	3	2	3	3	1	2	16
	6.3	6.3	18.8	12.5	18.8	18.8	6.3	12.5	100.0
	0.0	0.1	0.2	0.1	0.0	0.0	0.3	0.3	0.1
011	5	1	0	5	1	6	2	5	25
	20.0	4.0	0.0	20.0	4.0	24.0	8.0	20.0	100.0
	0.2	0.1	0.0	0.2	0.0	0.1	0.7	0.6	0.1
100	1,185	517	1,531	555	7,774	1,479	187	139	13,367
	8.9	3.9	11.5	4.2	58.2	11.1	1.4	1.0	100.0
	47.3	34.4	81.5	21.0	85.8	15.0	63.6	17.5	46.8
101	1,040	851	234	1,889	849	7,893	42	426	13,224
	7.9	6.4	1.8	14.3	6.4	59.7	0.3	3.2	100.0
	41.6	56.7	12.5	71.6	9.4	79.8	14.3	53.6	46.3
110	14	5	17	12	15	9	39	11	122
	11.5	4.1	13.9	9.8	12.3	7.4	32.0	9.0	100.0
	0.6	0.3	0.9	0.5	0.2	0.1	13.3	1.4	0.4
111	61	16	2	44	12	100	10	187	432
	14.1	3.7	0.5	10.2	2.8	23.2	2.3	43.3	100.0
	2.4	1.1	0.1	1.7	0.1	1.0	3.4	23.5	1.5
Total	2,503	1,501	1,879	2,638	9,058	9,896	294	795	28,564
	8.8	5.3	6.6	9.2	31.7	34.7	1.0	2.8	100.0
	100.0	100.0	100.0	100.0	100.0	100.0	100.0	100.0	100.0

Notes:

The first digit indicates the use of a Restricted ACE inhibitor (=1), or not (=0), the second indicates the use of an Unrestricted ACE inhibitor, and the third digit indicates use of a substitute drug.

Period of pre-RP use: 114 day period ending October 27, 1996; Period of post-RP use: 114 day period beginning April 1, 1997.

The first entry in each cell is the frequency, the second entry is the row percentage and the third entry, the column percentage.

Table 23 Cross tabulation of ACE inhibitor and substitute drug use before and after RP, by RP reimbursement status. Subsample of those taking unrestricted ACE inhibitors pre-RP.

Pre RP	Post RP								Total
	000	001	010	011	100	101	110	111	
000	53	9	107	66	1	1	2	4	243
	21.8	3.7	44.0	27.2	0.4	0.4	0.8	1.7	100.0
	7.7	2.6	4.6	1.9	2.0	0.8	5.9	1.5	3.3
001	15	22	16	91	1	3	0	8	156
	9.6	14.1	10.3	58.3	0.6	1.9	0.0	5.1	100.0
	2.2	6.3	0.7	2.6	2.0	2.3	0.0	3.0	2.1
010	256	84	1,905	457	25	19	13	18	2,777
	9.2	3.0	68.6	16.5	0.9	0.7	0.5	0.7	100.0
	37.3	23.9	81.9	13.2	49.0	14.6	38.2	6.8	37.9
011	305	223	285	2,801	8	65	1	63	3,751
	8.1	6.0	7.6	74.7	0.2	1.7	0.0	1.7	100.0
	44.5	63.5	12.3	80.6	15.7	50.0	2.9	23.7	51.2
100	1	2	4	2	3	1	0	0	13
	7.7	15.4	30.8	15.4	23.1	7.7	0.0	0.0	100.0
	0.2	0.6	0.2	0.1	5.9	0.8	0.0	0.0	0.2
101	2	1	1	10	1	8	0	6	29
	6.9	3.5	3.5	34.5	3.5	27.6	0.0	20.7	100.0
	0.3	0.3	0.0	0.3	2.0	6.2	0.0	2.3	0.4
110	2	2	4	6	4	4	13	9	44
	4.6	4.6	9.1	13.6	9.1	9.1	29.6	20.5	100.0
	0.3	0.6	0.2	0.2	7.8	3.1	38.2	3.4	0.6
111	52	8	4	43	8	29	5	158	307
	16.9	2.6	1.3	14.0	2.6	9.5	1.6	51.5	100.0
	7.6	2.3	0.2	1.2	15.7	22.3	14.7	59.4	4.2
Total	686	351	2,326	3,476	51	130	34	266	7,320
	9.4	4.8	31.8	47.5	0.7	1.8	0.5	3.6	100.0
	100.0	100.0	100.0	100.0	100.0	100.0	100.0	100.0	100.0

Notes:

The first digit indicates the use of a Restricted ACE inhibitor (=1), or not (=0), the second indicates the use of an Unrestricted ACE inhibitor, and the third digit indicates use of a substitute drug.

Period of pre-RP use: 114 day period ending October 27, 1996; Period of post-RP use: 114 day period beginning April 1, 1997.

The first entry in each cell is the frequency, the second entry is the row percentage and the third entry, the column percentage.

Table 24 Cross tabulation of CCB and substitute drug use before and after RP, by RP reimbursement status. Subsample of those taking restricted CCBs pre-RP.

Pre RP	Post RP								Total
	000	001	010	011	100	101	110	111	
000	64	30	20	9	162	75	4	1	365
	17.5	8.2	5.5	2.5	44.4	20.6	1.1	0.3	100.0
	5.6	2.7	3.3	1.3	3.3	1.3	4.8	0.8	2.5
001	16	30	1	9	26	95	1	3	181
	8.8	16.6	0.6	5.0	14.4	52.5	0.6	1.7	100.0
	1.4	2.7	0.2	1.3	0.5	1.7	1.2	2.3	1.3
010	0	1	1	0	1	0	0	0	3
	0.0	33.3	33.3	0.0	33.3	0.0	0.0	0.0	100.0
	0.0	0.1	0.2	0.0	0.0	0.0	0.0	0.0	0.0
011	0	0	0	1	0	3	0	0	4
	0.0	0.0	0.0	25.0	0.0	75.0	0.0	0.0	100.0
	0.0	0.0	0.0	0.2	0.0	0.1	0.0	0.0	0.0
100	640	440	517	134	4,305	860	68	41	7,005
	9.1	6.3	7.4	1.9	61.5	12.3	1.0	0.6	100.0
	56.1	39.0	84.3	20.0	86.3	15.4	81.0	30.8	48.8
101	410	623	65	508	490	4,547	11	85	6,739
	6.1	9.2	1.0	7.5	7.3	67.5	0.2	1.3	100.0
	36.0	55.2	10.6	75.8	9.8	81.4	13.1	63.9	47.0
110	1	0	5	1	3	0	0	0	10
	10.0	0.0	50.0	10.0	30.0	0.0	0.0	0.0	100.0
	0.1	0.0	0.8	0.2	0.1	0.0	0.0	0.0	0.1
111	9	4	4	8	1	6	0	3	35
	25.7	11.4	11.4	22.9	2.9	17.1	0.0	8.6	100.0
	0.8	0.4	0.7	1.2	0.0	0.1	0.0	2.3	0.2
Total	1,140	1,128	613	670	4,988	5,586	84	133	14,342
	8.0	7.9	4.3	4.7	34.8	39.0	0.6	0.9	100.0
	100.0	100.0	100.0	100.0	100.0	100.0	100.0	100.0	100.0

Notes:

The first digit indicates the use of a Restricted CCB (=1), or not (=0), the second indicates the use of an Unrestricted CCB, and the third digit indicates use of a substitute drug.

Period of pre-RP use: 114 day period ending October 27, 1996; Period of post-RP use: 114 day period beginning April 1, 1997.

The first entry in each cell is the frequency, the second entry is the row percentage and the third entry, the column percentage.

Table 25 Cross tabulation of CCB and substitute drug use before and after RP, by RP reimbursement status. Subsample of those taking unrestricted CCBs pre-RP.

Pre RP	Post RP								Total
	000	001	010	011	100	101	110	111	
000	73	32	253	129	1	5	1	0	494
	14.8	6.5	51.2	26.1	0.2	1.0	0.2	0.0	100.0
	4.8	2.8	3.2	1.4	1.9	2.5	5.6	0.0	2.5
001	16	29	33	174	0	3	1	1	257
	6.2	11.3	12.8	67.7	0.0	1.2	0.4	0.4	100.0
	1.1	2.5	0.4	1.9	0.0	1.5	5.6	1.1	1.3
010	743	382	6,635	1,531	28	34	12	18	9,383
	7.9	4.1	70.7	16.3	0.3	0.4	0.1	0.2	100.0
	49.1	33.1	84.4	16.7	51.9	16.9	66.7	19.2	46.7
011	669	702	923	7,306	15	132	3	55	9,805
	6.8	7.2	9.4	74.5	0.2	1.4	0.0	0.6	100.0
	44.3	60.9	11.7	79.5	27.8	65.7	16.7	58.5	48.8
100	0	1	4	4	2	0	0	0	11
	0.0	9.1	36.4	36.4	18.2	0.0	0.0	0.0	100.0
	0.0	0.1	0.1	0.0	3.7	0.0	0.0	0.0	0.1
101	0	2	2	11	0	3	1	3	22
	0.0	9.1	9.1	50.0	0.0	13.6	4.6	13.6	100.0
	0.0	0.2	0.0	0.1	0.0	1.5	5.6	3.2	0.1
110	3	0	6	5	6	0	0	1	21
	14.3	0.0	28.6	23.8	28.6	0.0	0.0	4.8	100.0
	0.2	0.0	0.1	0.1	11.1	0.0	0.0	1.1	0.1
111	8	5	4	34	2	24	0	16	93
	8.6	5.4	4.3	36.6	2.2	25.8	0.0	17.2	100.0
	0.5	0.4	0.1	0.4	3.7	11.9	0.0	17.0	0.5
Total	1,512	1,153	7,860	9,194	54	201	18	94	20,086
	7.5	5.7	39.1	45.8	0.3	1.0	0.1	0.5	100.0
	100.0	100.0	100.0	100.0	100.0	100.0	100.0	100.0	100.0

Notes:

The first digit indicates the use of a Restricted CCB (=1), or not (=0), the second indicates the use of an Unrestricted CCB, and the third digit indicates use of a substitute drug.

Period of pre-RP use: 114 day period ending October 27, 1996; Period of post-RP use: 114 day period beginning April 1, 1997.

The first entry in each cell is the frequency, the second entry is the row percentage and the third entry, the column percentage.

4.2.3 Mortality

We described annual mortality rates, by drug category, after the introduction of RP, by RP exposure status: Restricted drug users pre-RP (potentially exposed to RP) and Unrestricted drug users pre-RP (comparators). These rates are unadjusted for confounding variables – i.e. those variables correlated with RP exposure status and mortality, and are reported for descriptive purposes. All subjects who died prior to the introduction of RP were removed. (Recall subjects were selected on the basis of drug use prior to the RP announcement date, and some could have died in the intervening period.)

Most subjects who died after the introduction of RP passed away from a cardiovascular or renal (hereafter ‘CVD’) related condition as opposed to all other conditions. For nitrates users, rates of CVD related death (averaged over all RP exposure types) were over twice as high as rates from all other causes (7.2 persons per year vs. 2.9 persons per year). The ratio of CVD-related vs. all other death rates were slightly smaller for ACE inhibitor users (4.0 vs. 2.4) and for CCB users (2.5 vs. 1.9).

The differences in the CVD mortality rates between those exposed and not exposed to RP varied by drug class. Among nitrates users, Restricted drug users faced slightly higher death rates, while among ACE inhibitors and CCB users, Unrestricted drug users had higher death rates. With the exception of the ACE inhibitors users, however, all differences were not statistically different from zero as the respective confidence intervals overlapped. The Kaplan-Meier post-RP survival and cumulative hazard estimates (Figures 21-26) corroborate this finding. Users of Unrestricted ACE inhibitors had statistically higher death rates than did Restricted ACE inhibitor users.

Table 26 Annual unadjusted mortality rates, by RP drug group, cause of death, and RP exposure status, with 95% confidence intervals.

Drug Group	Cause of Death	RP Exposure Status	Person-years	Relative Freq.	Mortality Rate*100	95% C.I.	
Nitrates	Cardiovascular & Renal	Restricted drug pre-RP	21,007	86.2	7.3	7.0	7.7
		UR drug pre-RP	3,364	13.8	6.5	5.7	7.5
		Total	24,371	100.0	7.2	6.9	7.6
	All other	Restricted drug pre-RP	21,007	86.2	3.0	2.8	3.2
		UR drug pre-RP	3,364	13.8	2.6	2.1	3.2
		Total	24,371	100.0	2.9	2.7	3.2
ACE inhibitors	Cardiovascular & Renal	R drug pre-RP	27,101	79.8	3.8	3.6	4.0
		UR drug pre-RP	6,856	20.2	4.7	4.3	5.3
		Total	33,957	100.0	4.0	3.8	4.2
	All other	R drug pre-RP	27,101	79.8	2.2	2.1	2.4
		UR drug pre-RP	6,856	20.2	3.0	2.6	3.4
		Total	33,957	100.0	2.4	2.2	2.6
CCBs	Cardiovascular & Renal	R drug pre-RP	13,803	41.8	2.3	2.1	2.6
		UR drug pre-RP	19,240	58.2	2.7	2.5	2.9
		Total	33,043	100.0	2.5	2.4	2.7
	All other	R drug pre-RP	13,803	41.8	1.8	1.6	2.0
		UR drug pre-RP	19,240	58.2	2.0	1.8	2.2
		Total	33,043	100.0	1.9	1.7	2.0

Figure 21 Kaplan-Meier survival estimates (death due to cardiovascular and renal-related conditions), by Nitrates RP exposure status (users of Restricted vs. of Unrestricted drugs pre-RP)

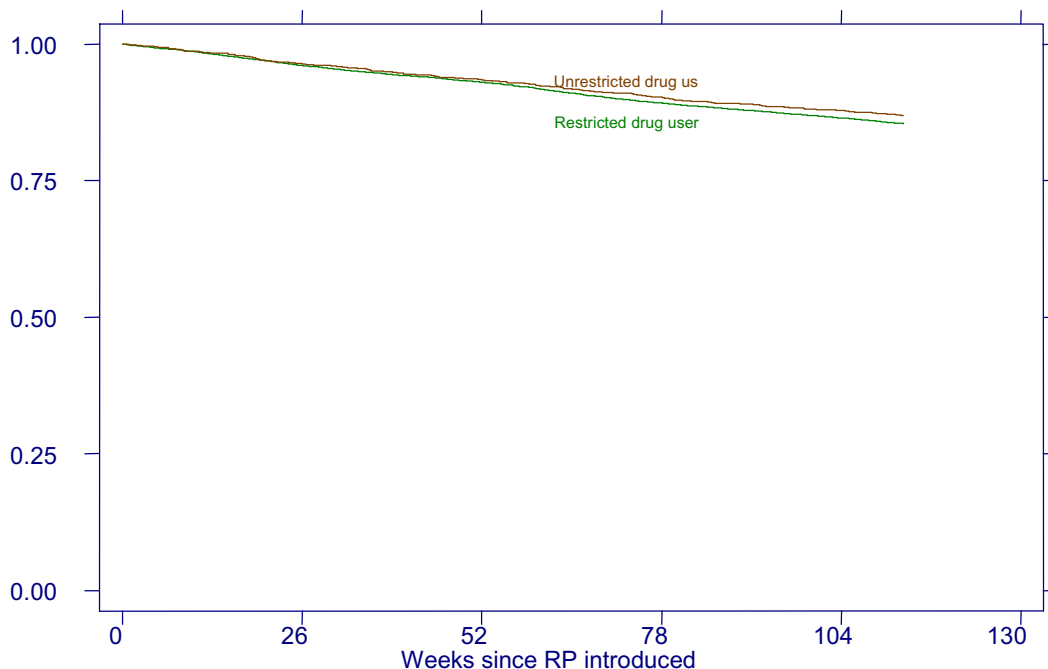


Figure 22 Cumulative hazard estimates (death due to cardiovascular and renal-related conditions), by Nitrates RP exposure status (users of Restricted vs. of Unrestricted drugs pre-RP)

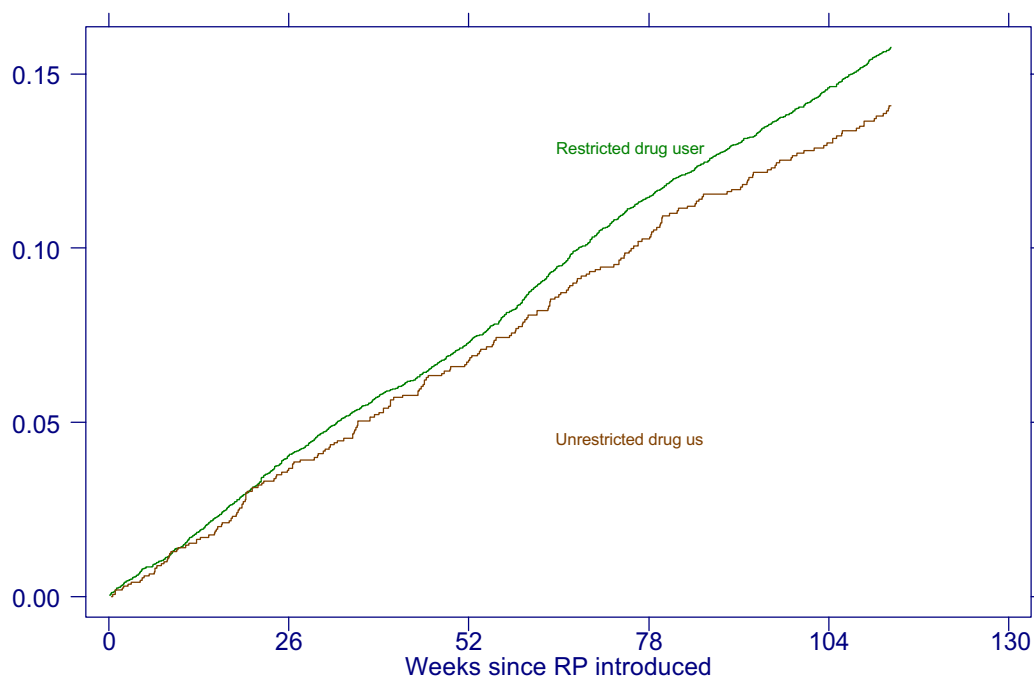


Figure 23 Kaplan-Meier survival estimates (death due to cardiovascular and renal-related conditions), by ACE inhibitor RP exposure status (users of Restricted vs. of Unrestricted drugs pre-RP)

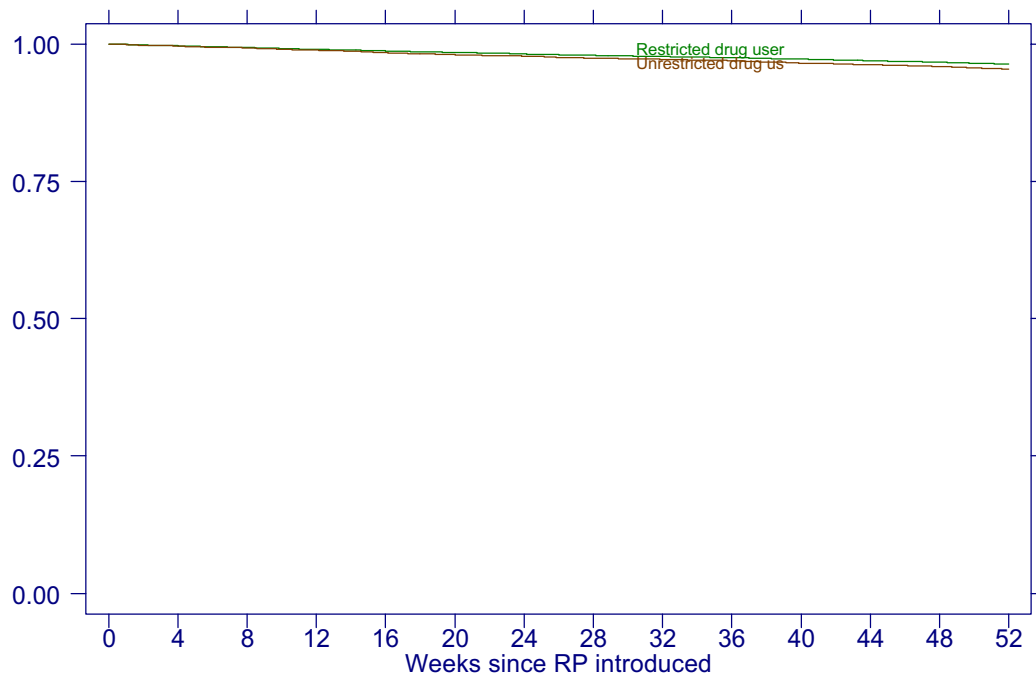


Figure 24 Cumulative hazard estimates (death due to cardiovascular and renal-related conditions), by ACE inhibitor RP exposure status (users of Restricted vs. of Unrestricted drugs pre-RP)

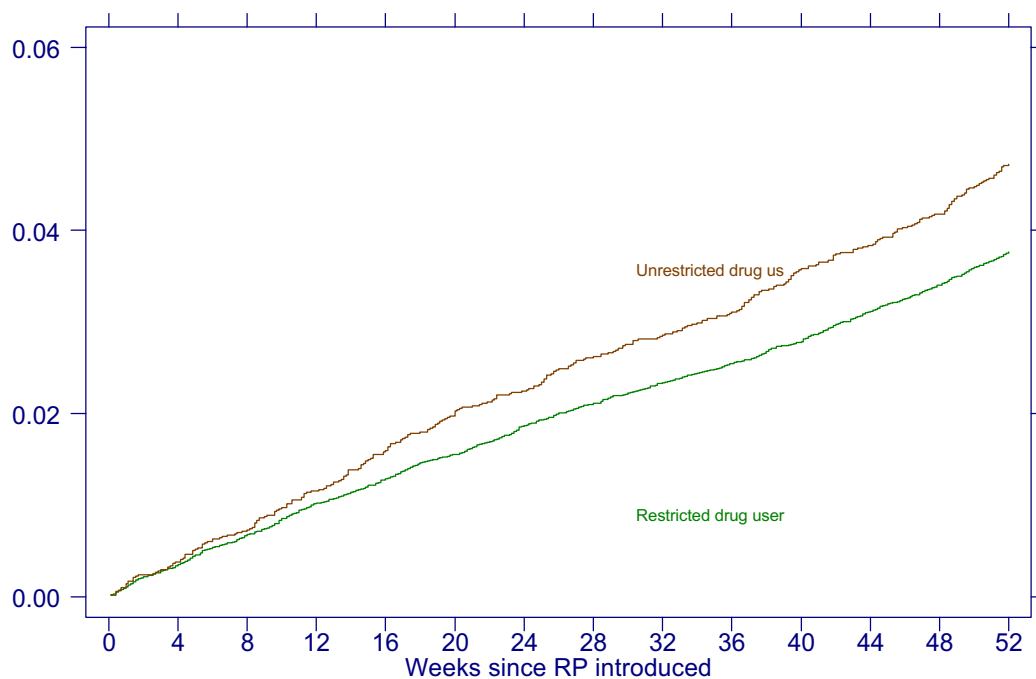


Figure 25 Kaplan-Meier survival estimates (death due to cardiovascular and renal-related conditions), by CCB RP exposure status (users of Restricted vs. Unrestricted drugs pre-RP)

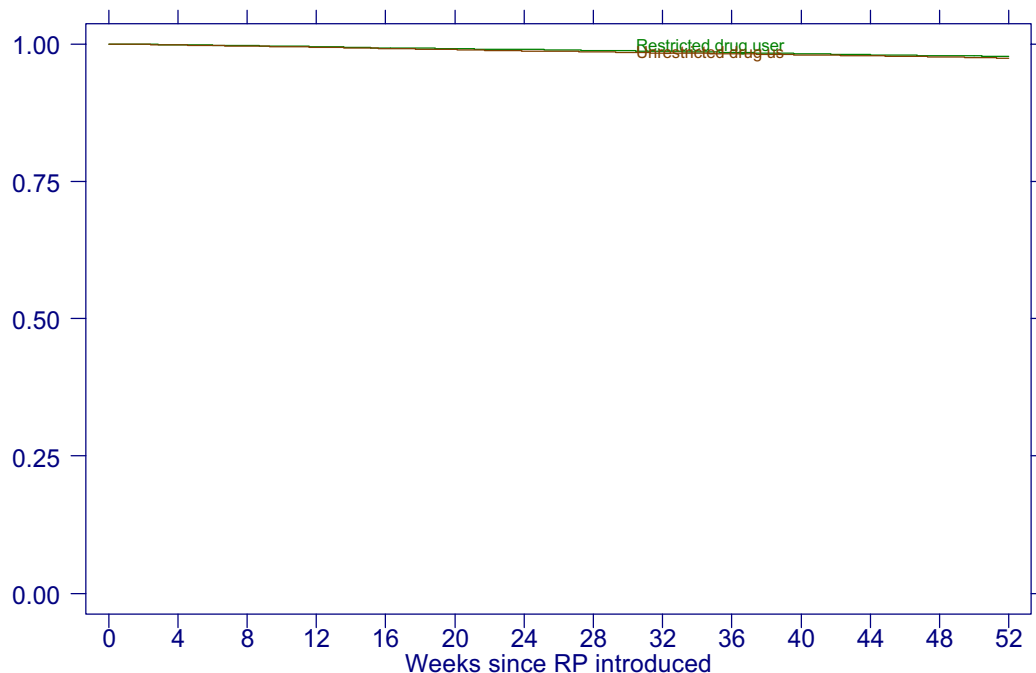
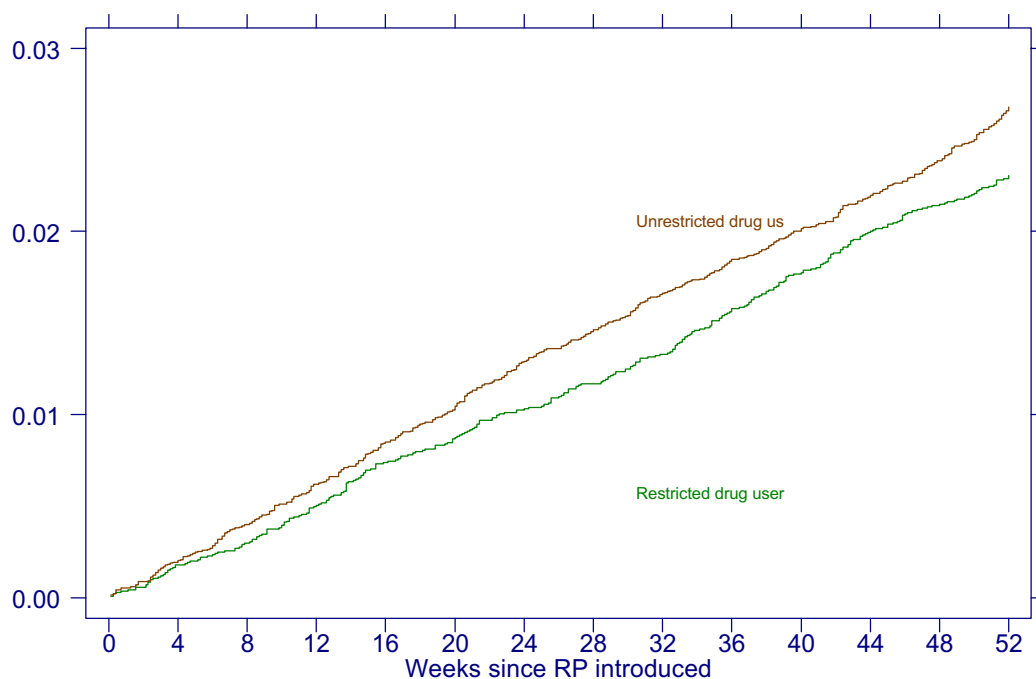


Figure 26 Cumulative hazard estimates (death due to cardiovascular and renal-related conditions), by CCB RP exposure status (users of Restricted vs. Unrestricted drugs pre-RP)

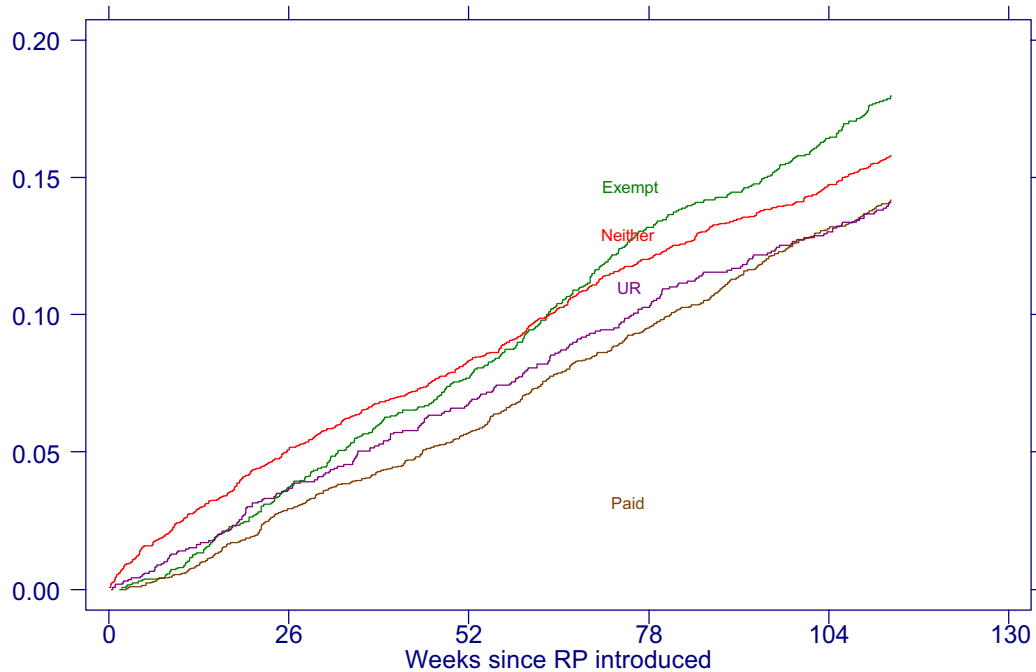


4.2.4 *Sample selection bias using an alternative definition of exposure to RP*

Recall that we elected to define RP exposure using solely pre-RP drug use data owing to the possibility of sample selection bias. In particular, had we defined exposure on the basis of whether those who used a Restricted drug pre-RP, stopped using such a drug post-RP, then we could have also captured those subjects who died (for reasons other than RP) prior to being able to use Restricted drugs post-RP.

Figures 27-29 provide some evidence that sample selection bias would have been a problem. Within the group of Restricted drug users, we distinguished those who received exemptions for all Restricted drugs dispensed post-RP ('Exempted'); those who paid for all Restricted drugs post-RP and/or paid for some drugs and received exemption for others ('Paid'); and those who did not take Restricted drugs post-RP ('Neither'). Those who used Unrestricted drugs pre-RP were labeled 'UR'. In each drug group, those who were not dispensed Restricted drugs post-RP had higher death rates within the first 20 weeks post policy than the other groups. This is highly suggestive of selection bias because it is unlikely that RP-induced deteriorations in health would result in death in such a short time after the introduction of the policy. Indeed, as is clear from earlier analysis of aggregate drug use, many subjects stockpiled Restricted drugs pre-RP and would not have been forced to disrupt drug therapy until up to 100 days (about 15 weeks) post-RP. Further evidence of selection bias is apparent from Figure 30; here we plot the cumulative hazard estimates of those who used Restricted ACE inhibitors pre-RP, but did not after the introduction of RP, by their post-RP switching status (an indicator of whether they switched from a Restricted to Unrestricted ACE inhibitor or substitute post-RP). Those who did not switch presumably stopped using ACE inhibitors altogether and/or died. Non-switchers faced very high hazards within the first 12 weeks post-RP; it seems implausible that this is solely the result of a disruption in their drug use.

Figure 27 Cumulative hazard estimates (death due to cardiovascular and renal-related conditions), by Nitrates RP exposure status (exempted, paid, neither, and users of Unrestricted drugs pre-RP)



Note: 'exempt' includes those who used Restricted drugs pre-RP who received exemption for all Restricted drugs taken post-RP; 'paid' includes those used Restricted drugs pre-RP who paid for all Restricted drugs post-RP or received exemption for some Restricted drugs taken post-RP; 'neither' includes those who did not receive prescriptions of Restricted drugs post-RP; 'UR' includes those who used Unrestricted drugs pre-RP.

Figure 28 Cumulative hazard estimates (death due to cardiovascular and renal-related conditions), by ACE inhibitor RP exposure status (exempted, paid, neither, and users of Unrestricted drugs pre-RP)

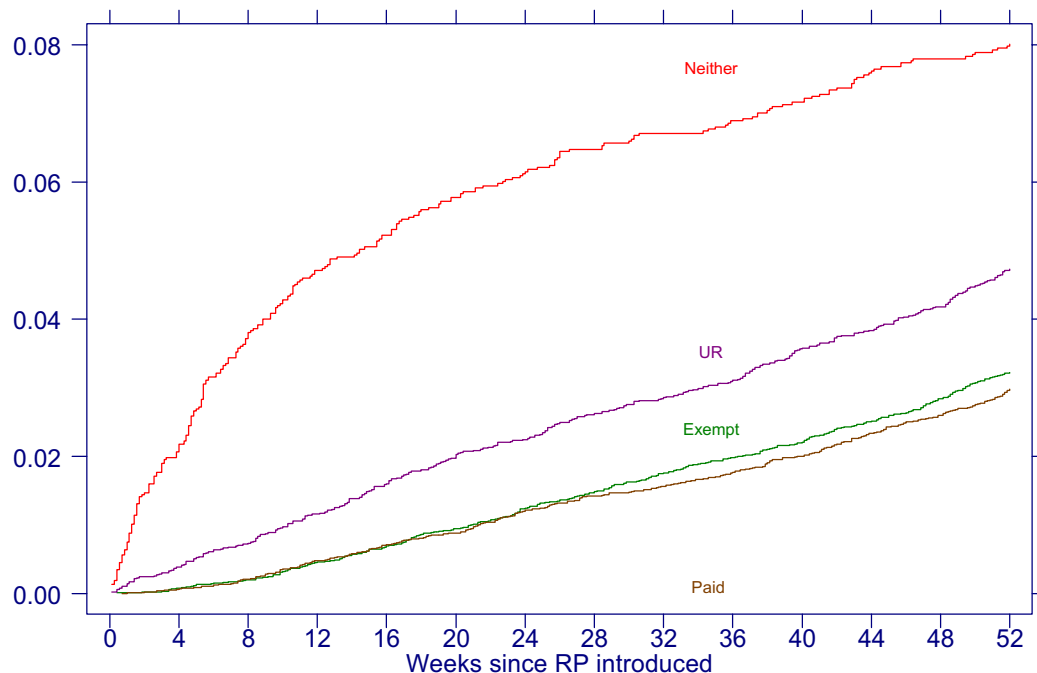


Figure 29 Cumulative hazard estimates (death due to cardiovascular and renal-related conditions), by CCB RP exposure status (exempted, paid, neither, and users of Unrestricted drugs pre-RP)

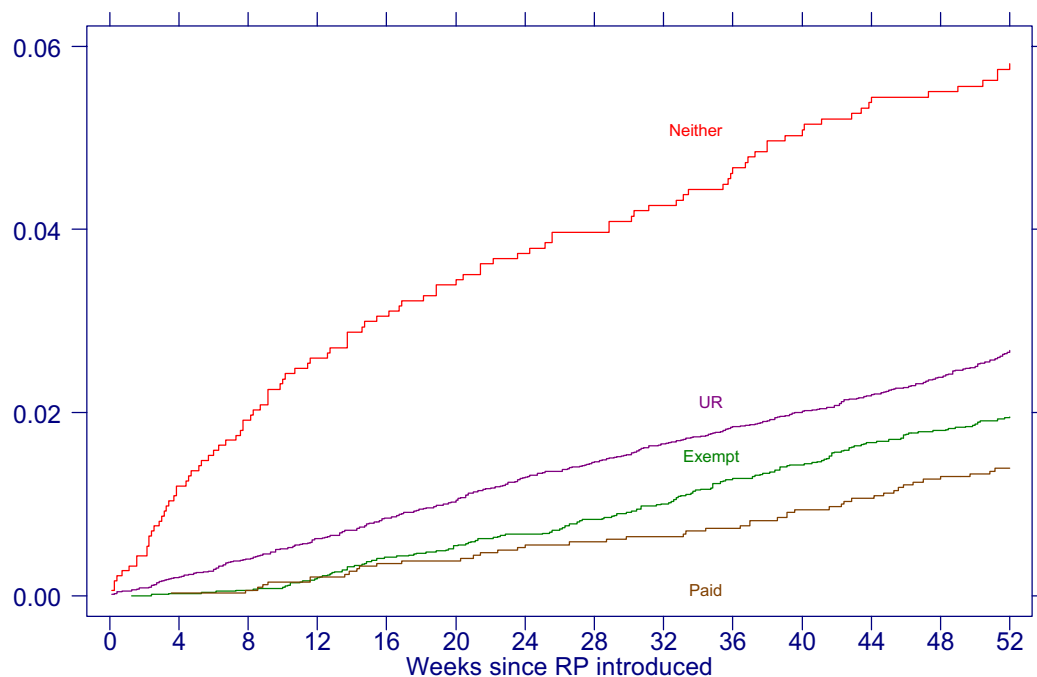
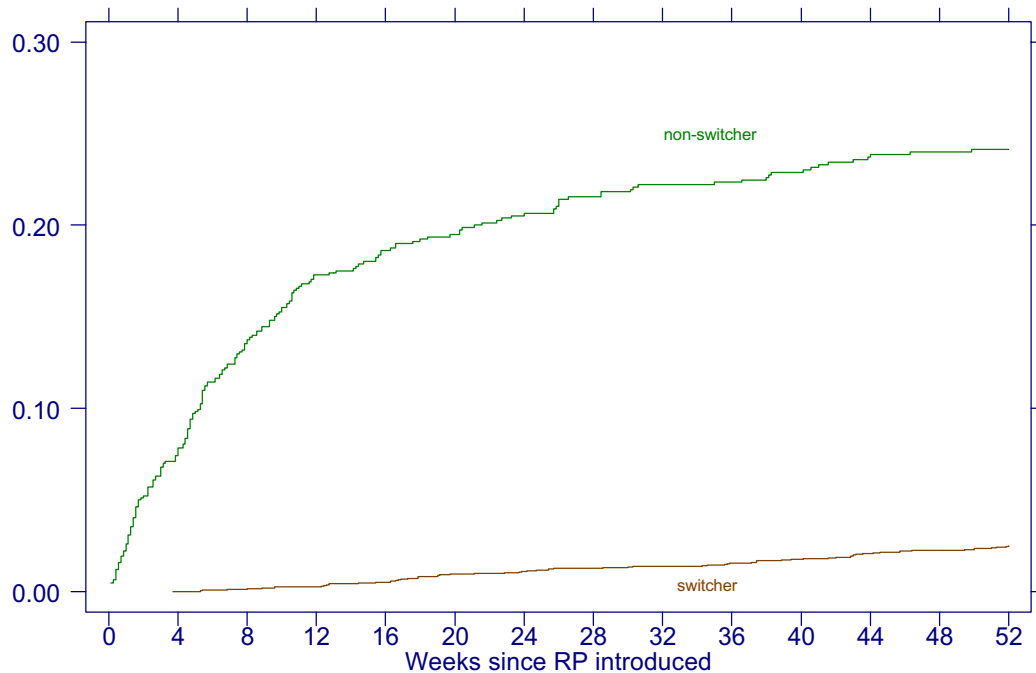


Figure 30 Cumulative hazard estimates (death due to cardiovascular and renal-related conditions), among those who were dispensed Restricted ACE inhibitors pre-RP, but not post RP, by their post-RP switching status



Note: Sample restricted to those who used Restricted drugs pre-RP, and stopped using them post-RP. 'Switcher' includes those who initiated therapy on an Unrestricted ACE inhibitor or substitute post-RP. 'Non-switchers' did not initiate therapy on an Unrestricted ACE inhibitor or substitute post-RP.

We next estimated the effect of RP exposure status (Restricted vs. Unrestricted drug users) on CVD-related mortality. First, we compared the 1 year mortality of the two groups over two different periods – the year following RP and the year preceding RP. The former estimate reflects just the effects of baseline differences between the exposed and comparator group on mortality, whereas the latter estimate reflects both the effect of RP and baseline differences on mortality. Hence the difference between the 2 hazard ratio estimates should indicate the difference due to RP alone. Hazard ratios were estimated using Cox proportional hazards regression, with no other covariates besides RP exposure status. For nitrates and CCB users, there is no difference in hazard rates. There is a small effect for the ACE inhibitor users – the hazard ratio was 7 percentage points larger in the post-RP period than in the year before RP (Figure 31 and Table 27), although the effect was not statistically significant at the 5% level.

Figure 31 Estimated hazard ratio for cardiovascular and renal related death, with 95% confidence intervals, 1 year pre- and 1 year post reference pricing, by drug group

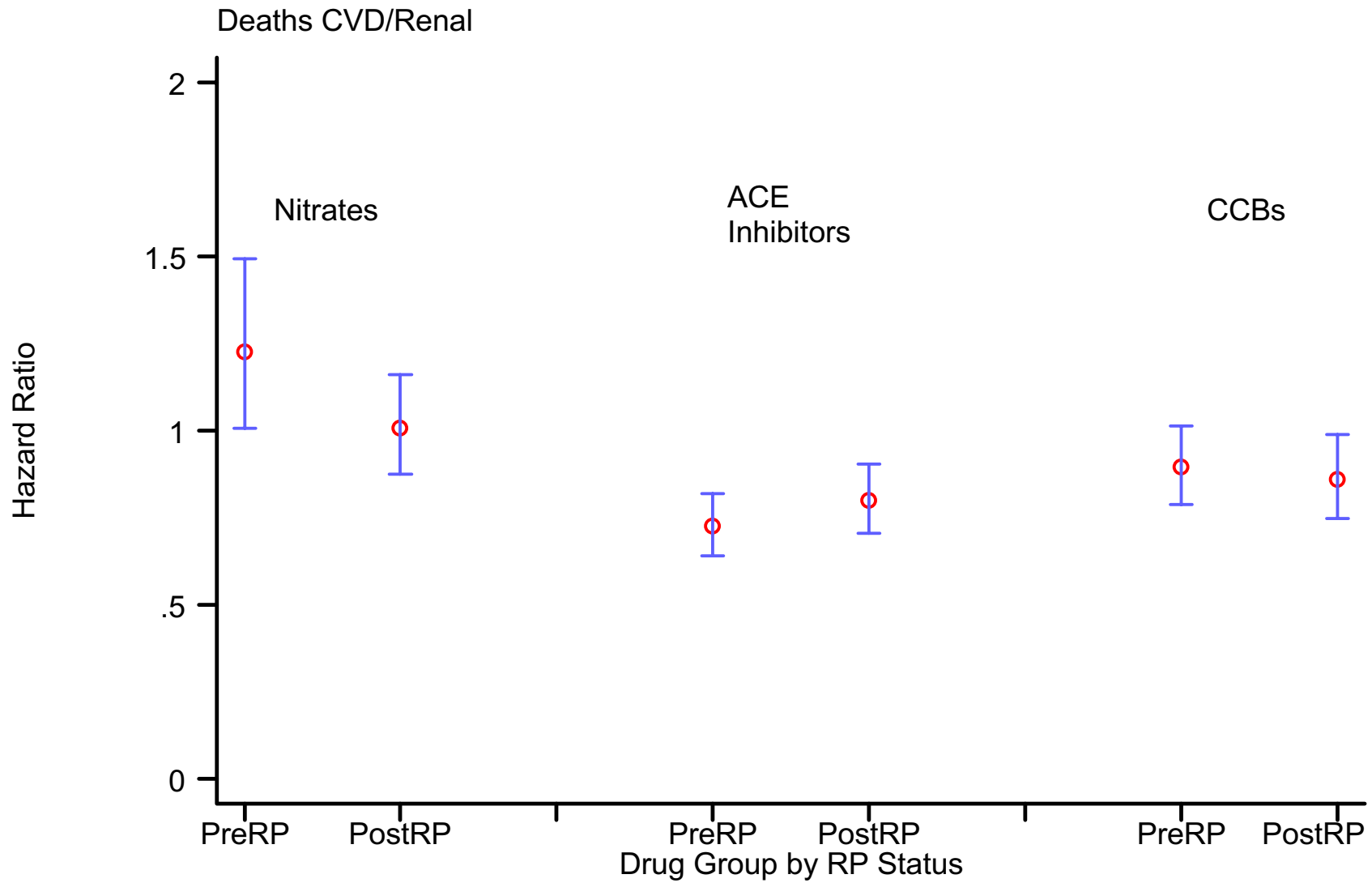


Table 27 Estimated hazard ratio for cardiovascular and renal related death, with 95% confidence intervals, 1 year pre- and 1 year post reference pricing, by drug group

Drug group	Comparison of 1 year hazard of CVD related death between Restricted vs. Unrestricted drug users at:						Absolute difference in hazard ratios
	RP introduction			1 year before RP			
	Hazard ratio	95% confidence interval		Hazard ratio	95% confidence interval		
Nitrates	1.007	0.875	1.161	1.225	1.006	1.492	-0.218
ACE inhibitor	0.798	0.704	0.904	0.725	0.640	0.820	0.073
CCBs	0.860	0.748	0.989	0.894	0.788	1.013	-0.034

To corroborate these results, we also estimated Cox proportional hazards models of post-RP death from CVD related conditions, using as covariates an indicator of RP exposure status, and a set of regressors indicating the use of a variety of health services in the year prior to the introduction of RP, as well as patient age, sex and low income status. In some models, the proportional hazards assumption appeared to be violated. We therefore re-estimated using the generalized gamma model (this model relaxes the PH assumption) to ensure results were robust. The results appear in Table 28 below.

For the nitrates, ACE inhibitor and CCB users, there is no evidence that Restricted drugs users were at higher risk for CVD related death than Unrestricted drug users. The hazard rate for the Restricted ACE inhibitor drug users is about 3.7 times that of the Unrestricted drug users, but there is no statistical difference between these rates at the 5% level (the p -value associated with the test was 0.11). The same is true for the time ratio estimated using the generalized gamma regression – those using Restricted drugs pre-RP have post-RP survival of only 29% of the survival of the Unrestricted drug users, but the p -value is even larger than for the Cox model ($p=0.27$).

Table 28 Estimates of RP Exposure on post-RP CVD mortality, by drug group, and estimator type

Drug Group	Estimation Method	Statistic	Estimate	P Value	95% Confidence Interval	
Nitrates	Cox P. H.	Haz. Ratio	0.72	0.52	0.26	1.97
	Gen. Gamma	Time Ratio	1.26	0.68	0.42	3.83
ACE inhibitors	Cox P. H.	Haz. Ratio	3.70	0.11	0.76	18.11
	Gen. Gamma	Time Ratio	0.29	0.27	0.03	2.65
CCBs	Cox P. H.	Haz. Ratio	0.95	0.79	0.67	1.35
	Gen. Gamma	Time Ratio	1.05	0.81	0.73	1.50

4.2.5 Longterm care admissions

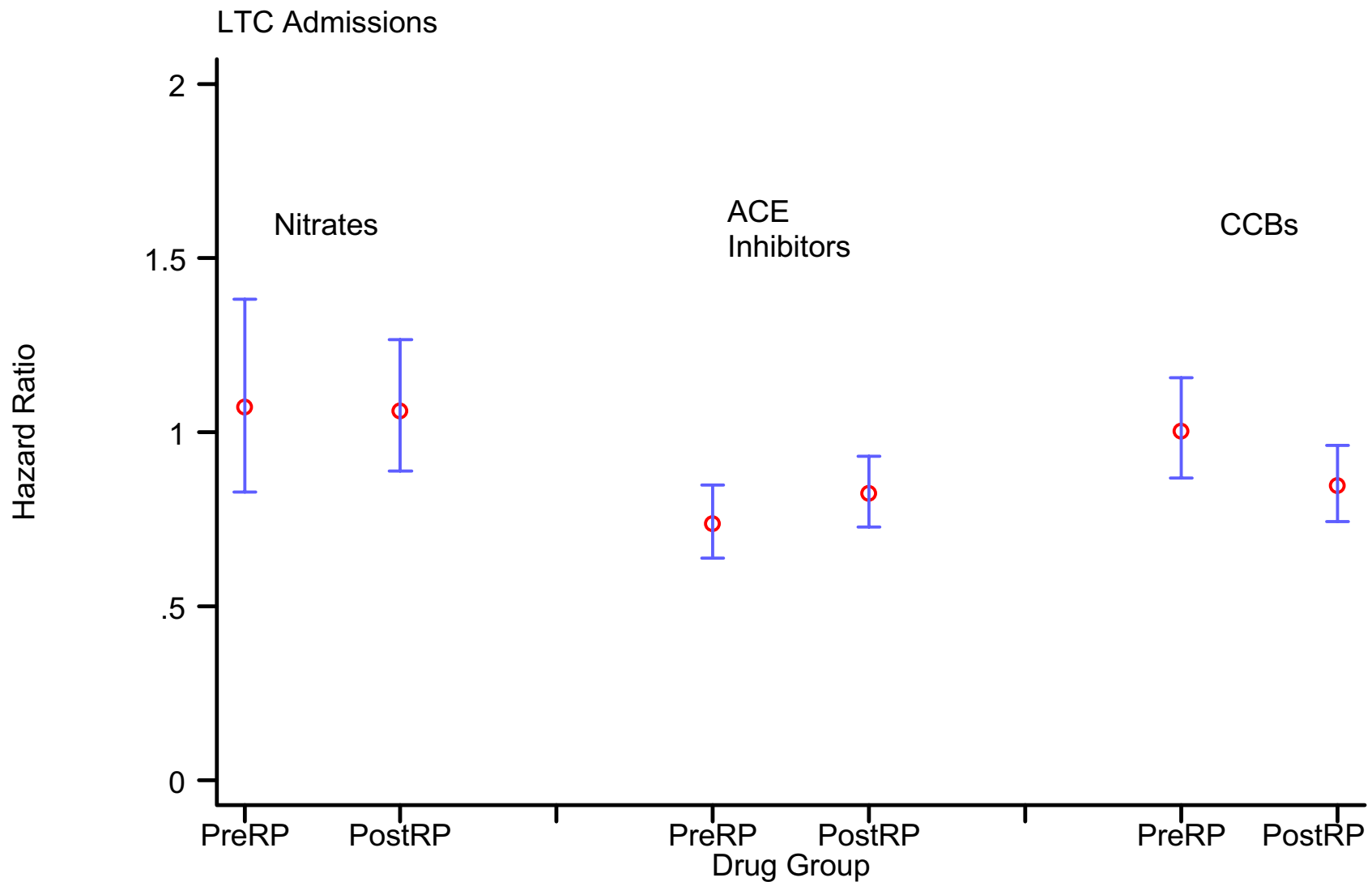
We next estimated the effect of RP exposure status (Restricted vs. Unrestricted drug users) on time to longterm care admission. As with the analysis of time to death, to ensure that our results

were robust we estimated using two different approaches. The first analysis compared the 1 year mortality of the two groups over two different periods – the year following RP and the year preceding RP. These estimates are reported in Table 29 and displayed graphically in Figure 32. For nitrates, ACE inhibitor, and CCB users there is no difference in hazard rates. There is a small effect for the ACE inhibitor users – the hazard ratio was 8.7 percentage points larger in the post-RP period than in the year before RP, but the effect is statistically insignificant at the 5% level.

Table 29 Cox proportional hazard ratio estimates of RP exposure status and RP exposure status 1 year prior to RP, on time to admission to a longterm care facility, by drug group

Drug group	Comparison of 1 year hazard of LTC admission between Restricted vs. Unrestricted drug users at:						Absolute difference in hazard ratios
	RP introduction			1 year before RP			
	Hazard ratio	95% confidence interval		Hazard ratio	95% confidence interval		
Nitrates	1.060	0.888	1.266	1.070	0.829	1.382	-0.010
ACE inhibitor inhibitors	0.823	0.727	0.931	0.736	0.639	0.849	0.087
CCBs	0.846	0.744	0.962	1.002	0.868	1.157	-0.156

Figure 32 Estimated hazard ratio for longterm care facility admission, with 95% confidence intervals, 1 year pre- and 1 year post reference pricing, by drug group



The Cox models of time to longterm care admission were generally consistent with the PH assumption, and hence we did not estimate using a fully parametric model. The regressors used for the Cox models of CVD mortality were used here as well. Results are available only for the nitrates and CCB users; models we estimated for ACE inhibitor users were not able to identify the effects of RP due to suspected collinearity with the control regressors. Overall, in the models estimated, we could find no evidence that RP exposure was associated with post-RP time to admission to longterm care.

Table 30 Estimates of effect of nitrates RP Exposure on hazard of post-RP admission to Longterm care facility, by drug group

Drug Group	Hazard Ratio Estimate	P Value	95% Confidence Interval	
Nitrates	1.32	0.70	0.32	5.47
ACE inhibitors	Not identified			
CCBs	0.79	0.20	0.55	1.13

4.2.6 Physician and hospital services, and sublingual nitroglycerin use

To identify the effects of RP on morbidity for those taking Restricted drugs pre-RP, we needed to distinguish the effects of time-varying confounders from the effects due to RP. The effects of time-varying confounders were estimated by the pre-post RP difference in outcomes of those taking Unrestricted drugs pre-RP. Our approach is valid if the two groups are affected by the same time varying confounders. This assumption was formally tested by comparing the pre-RP trends in morbidity variables of the exposed and nonexposed groups. Using data ending the month prior to the introduction of RP, we obtained fixed effects linear regression estimates of both the trend estimate for the baseline group (non exposed subjects) and the interaction between the trend and an indicator of subjects who were exposed to RP. In general, the test results, reported in Table 31, support the use of the difference-in-differences design. The exceptions were the models of: the number of physician CVD diagnostic services for both nitrate and ACE inhibitor users, the hospital admissions and length of stay for ACE inhibitor users, and physician hospital and emergency room consults for CCB users.

Table 31 Results of *t*-tests of the equivalence of pre-RP rates of change over time in morbidity variables between Restricted and Unrestricted drug users, by drug group and morbidity variable

Drug Group	Morbidity Variable	Trend estimate	P-value	Trend*Restricted drug user	
				Estimate	P-value
Nitrates	Hospital admissions for CVD and renal related conditions	0.0003	0.024	-0.0003	0.219
	Hospital days length of stay for CVD and renal related conditions	0.0021	0.337	-0.0023	0.339
	Number of revascularizations performed in hospital	0.0000	0.502	-0.0001	0.116
	Prescriptions for sublingual nitroglycerin	0.0001	0.865	0.0005	0.264
	Physician hospital and emergency room consults	0.0061	0.064	-0.0060	0.088
	Physician ambulatory consults	-0.0009	0.462	0.0004	0.737
	Physician CVD related surgical procedures	0.0002	0.281	-0.0003	0.080
	Physician CVD related diagnostic procedures	0.0006	0.574	-0.0022	0.045
ACE inhibitors	Hospital admissions for CVD and renal related conditions	0.0001	0.065	-0.0001	0.004
	Hospital days length of stay for CVD and renal related conditions	0.0006	0.080	-0.0013	0.001
	Number of revascularizations performed in hospital	0.0000	0.597	0.0000	0.223
	Prescriptions for sublingual nitroglycerin	0.0002	0.043	0.0000	0.859
	Physician hospital and emergency room consults	0.0011	0.357	-0.0011	0.401
	Physician ambulatory consults	-0.0135	0.000	0.0006	0.248
	Physician CVD related surgical procedures	-0.0001	0.413	0.0000	0.824
	Physician CVD related diagnostic procedures	-0.0014	0.000	0.0009	0.012
CCBs	Hospital admissions for CVD and renal related conditions	0.0001	0.035	-0.0001	0.169
	Hospital days length of stay for CVD and renal related conditions	0.0012	0.000	-0.0005	0.329

				Trend*Restricted drug user	
	Number of revascularizations performed in hospital	0.0000	0.001	0.0000	0.192
	Prescriptions for sublingual nitroglycerin	0.0001	0.111	0.0000	0.839
	Physician hospital and emergency room consults	0.0034	0.000	-0.0031	0.000
	Physician ambulatory consults	-0.0141	0.000	-0.0003	0.538
	Physician CVD related surgical procedures	0.0001	0.019	0.0000	0.862
	Physician CVD related diagnostic procedures	-0.0011	0.000	0.0002	0.584

We next present the results of the fixed effect models for the morbidity indicators. Both a short run and long run effect is estimated. The short run effect is interpreted as the change in the outcome over the first 4 months of the policy introduction relative to the longrun effect (which is defined as the average effect from the introduction of RP to the end of the sample period). Focusing on the models for which the difference-in-difference design does appear to be appropriate (Tables 32-34), our most robust finding is that exposure to RP increases the number of ambulatory physician consultations in both the short run and longrun (for both ACE inhibitor and CCB users) or in just the short run only (for nitrates users). This is also evident from the inspection of the graphs of the mean number of consultations by month and RP exposure group, displayed below. Based on the poisson models, the shortrun effect is about a 5% and 3% increase for the exposed ACE inhibitor and CCB users, respectively. The linear regression and logit models provided corroborating evidence. The short run effect of RP on nitrates users pointed in the same direction, although the evidence was slightly weaker as effects were observed in the linear regression and logit models only. The linear regression model estimated a short run effect of 0.074 additional visits per subject per month, which is about 9% of the average number of visits in the year before RP. The longer run effects were between 5%-11% for the ACE inhibitor users (depending on estimation method), and were between 4%-7% for the CCB users. The additional physician visits in both the shortrun and longrun are consistent with patients consulting their physicians to discuss treatment options, and possibly the monitoring of those patients whose medicines were changed. It is also possible that these additional consultations are due to additional morbidity.

There is evidence of a short run increase in the likelihood of use of sublingual nitroglycerin among nitrate users exposed to RP – the log odds ratio is 0.164, and hence the odds ratio is 1.18. This indicates that the odds of using sublingual nitroglycerin conditional on RP exposure are about 18% higher than without exposure. RP did not appear to increase the number of prescriptions of sublingual nitroglycerin filled, suggesting that the effect of RP is to increase the proportion of individuals using the drug in the short run, but not individuals’ ‘intensity’ of use.

In the longer run, there was no evidence that RP increased the use of sublingual nitroglycerin. Moreover, there was no evidence of either short run or long run increases in the use of sublingual nitroglycerin among ACE inhibitor or CCB users.

We found no evidence that RP resulted in long run increases in morbidity among ACE inhibitor and CCB users, at least in the models for which the difference-in-differences design appeared to be appropriate. Indeed, we obtained the surprising results that in the long run, morbidity, as measured by CVD-related hospitalization and physician services, was actually greater in those not exposed to RP. There were, however, two related health services for nitrates users in which a long run morbidity effect was observed – in the probability of a hospital-based revascularization and the probability of a CVD-related surgical procedure performed by a physician. The parameter estimates, 1.835 and 1.985, yield odds ratios of 6.27 and 7.28, respectively. Hence both models suggest that the longrun odds of revascularization increased after exposure to RP by an order of between 6 and 7. There were no corresponding increases in the frequency of revascularizations.

The short run effects of RP of nitrates on revascularization were more ambiguous. Based on the poisson model, there was a doubling of the rate of CVD-related surgical procedures provided by a physician for those exposed, relative to those not exposed, but at the same time there was a 57% *decrease* in the odds of any surgical procedures coupled with a 54% decrease in the odds of any revascularization for those exposed relative to those not exposed. Furthermore, there was some evidence of short run increases in the hospital length of stay for CVD related conditions and in the number of physician hospital and ER visits. These effects were observed in the poisson and logit models, but not in the linear regression models.

Among ACE inhibitor users, there is some evidence of a shortrun increase in the probability and number of CVD-related surgical procedures, (the odds of a procedure increases 80% and the frequency of surgical events increases 88%) and a bigger increase in the probability of hospital based revascularization (odds ratio of 2.5). There is much weaker evidence of shortrun effects on morbidity among CCB users – there was an 11% increase in hospital length of stay for CVD related conditions, but this effect was not observed in either the fixed effect regression of logit models.

In what follows, we estimate the costs associated with the additional ambulatory physician consultations only. We will leave the estimation of the effects of RP on costs of other types of physicians' services, sublingual nitroglycerin, and revascularization for future work.

Table 32 Estimated short and long run effect of Nitrates RP on morbidity, by morbidity variable, outcome (number of events vs. probability of event) and estimation method. (See notes to Table 33.)

Morbidity Variable (y)	Outcome modeled	Estimation Method	Estimate of effect of RP				Longrun effect of RP as % of pre-RP mean	
			Shortrun		Longrun		Pre-RP mean	%
			Estimate	P-value	Estimate	P-value		
Hospital admissions for CVD and renal related conditions	Mean y	F.E. poisson regression	1.081	0.467	0.582	0.000	Na	na
		F.E. linear regression	0.000	0.857	-0.007	0.000	0.025	-28
	Prob. y>0	F.E. logit regression	0.148	0.078	-0.268	0.000		
Hospital days length of stay for CVD and renal related conditions	Mean y	F.E. poisson regression	1.435	0.000	0.459	0.000	Na	na
		F.E. linear regression	0.041	0.095	-0.064	0.000	0.187	-34
	Prob. y>0	F.E. logit regression	0.145	0.080	-0.281	0.000		
Number of revascularizations performed in hospital	Mean y	F.E. poisson regression	1.043	0.896	0.669	0.095	Na	na
		F.E. linear regression	0.000	0.773	0.000	0.591	0.002	-16
	Prob. y>0	F.E. logit regression	-0.775	0.000	1.835	0.000		
Prescriptions for sublingual nitroglycerin	Mean y	F.E. poisson regression	1.087	0.147	0.912	0.008	Na	na
		F.E. linear regression	0.006	0.108	-0.006	0.009	0.085	-7
	Prob. y>0	F.E. logit regression	0.164	0.004	-0.058	0.077		
Physician hospital and emergency room consults	Mean y	F.E. poisson regression	1.197	0.000	0.587	0.000	Na	na
		F.E. linear regression	0.021	0.538	-0.078	0.000	0.455	-17
	Prob. y>0	F.E. logit regression	0.241	0.000	-0.298	0.000		
Physician ambulatory consults	Mean y	F.E. poisson regression	1.016	0.396	0.968	0.008	Na	na
		F.E. linear regression	0.074	0.000	-0.088	0.000	0.797	-11
	Prob. y>0	F.E. logit regression	0.115	0.000	-0.129	0.000		
Physician CVD related surgical procedures	Mean y	F.E. poisson regression	2.106	0.001	0.725	0.037	na	na
		F.E. linear regression	0.004	0.079	-0.001	0.490	0.003	-30
	Prob. y>0	F.E. logit regression	-0.839	0.000	1.985	0.000		
<i>Physician CVD related diagnostic procedures</i>	<i>Mean y</i>	<i>F.E. poisson regression</i>	<i>1.016</i>	<i>0.663</i>	<i>0.741</i>	<i>0.000</i>	<i>na</i>	<i>na</i>
		<i>F.E. linear regression</i>	<i>0.006</i>	<i>0.546</i>	<i>-0.049</i>	<i>0.000</i>	<i>0.182</i>	<i>-27</i>
	<i>Prob. y>0</i>	<i>F.E. logit regression</i>	<i>0.057</i>	<i>0.280</i>	<i>-0.207</i>	<i>0.000</i>		

Table 33 Estimated short and long run effect of ACE inhibitors RP on morbidity, by morbidity variable, outcome (number of events vs. probability of event) and estimation method. (See notes to Table 33.)

Morbidity Variable (y)	Outcome modeled	Estimation Method	Estimate of effect of RP				Longrun effect of RP as % of pre-RP mean	
			Shortrun		Longrun		Pre-RP mean	%
			Estimate	P-value	Estimate	P-value		
<i>Hospital admissions for CVD and renal related conditions</i>	Mean y	<i>F.E. poisson regression</i>	1.247	0.364	0.785	0.148	na	na
		<i>F.E. linear regression</i>	0.000	0.372	0.000	0.144	0.002	-27
	Prob. y>0	<i>F.E. logit regression</i>	0.373	0.000	-1.171	0.000		
<i>Hospital days length of stay for CVD and renal related conditions</i>	Mean y	<i>F.E. poisson regression</i>	1.374	0.000	0.515	0.000	na	na
		<i>F.E. linear regression</i>	0.008	0.221	-0.018	0.000	0.018	-101
	Prob. y>0	<i>F.E. logit regression</i>	0.156	0.112	-0.563	0.000		
Number of revascularizations performed in hospital	Mean y	<i>F.E. poisson regression</i>	0.000	0.986	0.096	0.001	na	na
		<i>F.E. linear regression</i>	0.000	0.004	0.000	0.003	0.000	0
	Prob. y>0	<i>F.E. logit regression</i>	0.910	0.000	-2.178	0.000		
Prescriptions for sublingual nitroglycerin	Mean y	<i>F.E. poisson regression</i>	0.959	0.632	0.991	0.879	na	na
		<i>F.E. linear regression</i>	0.000	0.799	0.000	0.622	0.015	-3
	Prob. y>0	<i>F.E. logit regression</i>	0.058	0.350	-0.446	0.000		
Physician hospital and emergency room consults	Mean y	<i>F.E. poisson regression</i>	1.019	0.299	0.900	0.000	na	na
		<i>F.E. linear regression</i>	0.007	0.734	-0.046	0.001	0.262	-18
	Prob. y>0	<i>F.E. logit regression</i>	0.067	0.120	-0.145	0.000		
Physician ambulatory consults	Mean y	<i>F.E. poisson regression</i>	1.047	0.031	1.112	0.000	na	na
		<i>F.E. linear regression</i>	0.017	0.029	0.032	0.000	0.628	5
	Prob. y>0	<i>F.E. logit regression</i>	0.079	0.007	0.117	0.000		
Physician CVD related surgical procedures	Mean y	<i>F.E. poisson regression</i>	1.881	0.021	0.465	0.000	na	na
		<i>F.E. linear regression</i>	0.001	0.246	-0.002	0.012	0.003	-70
	Prob. y>0	<i>F.E. logit regression</i>	0.591	0.000	-1.602	0.000		
<i>Physician CVD related diagnostic procedures</i>	Mean y	<i>F.E. poisson regression</i>	1.059	0.087	0.888	0.000	na	na
		<i>F.E. linear regression</i>	0.006	0.313	-0.012	0.002	0.115	-11
	Prob. y>0	<i>F.E. logit regression</i>	0.073	0.091	-0.203	0.000		

Table 34 Estimated short run and long run effect of CCB RP on morbidity, by morbidity variable, outcome (number of events vs. probability of event) and estimation method.

Morbidity Variable (y)	Outcome modeled	Estimation Method	Estimate of effect of RP				Longrun effect of RP as % of pre-RP mean	
			Shortrun		Longrun		Pre-RP mean	%
			Estimate	P-value	Estimate	P-value		
Hospital admissions for CVD and renal related conditions	Mean y	F.E. poisson regression	1.045	0.634	0.826	0.003	na	Na
		F.E. linear regression	0.000	0.636	-0.002	0.002	0.008	-24
	Prob. y>0	F.E. logit regression	0.056	0.414	-0.283	0.000		
Hospital days length of stay for CVD and renal related conditions	Mean y	F.E. poisson regression	1.109	0.001	0.652	0.000	na	Na
		F.E. linear regression	0.008	0.391	-0.033	0.000	0.059	-56
	Prob. y>0	F.E. logit regression	-0.018	0.794	-0.219	0.000		
Number of revascularizations performed in hospital	Mean y	F.E. poisson regression	1.394	0.113	0.863	0.403	na	Na
		F.E. linear regression	0.000	0.435	0.000	0.097	0.001	-47
	Prob. y>0	F.E. logit regression	0.171	0.072	-0.680	0.000		
Prescriptions for sublingual nitroglycerin	Mean y	F.E. poisson regression	0.995	0.936	1.050	0.225	na	Na
		F.E. linear regression	0.000	0.781	0.001	0.448	0.026	3
	Prob. y>0	F.E. logit regression	-0.145	0.006	0.010	0.756		
Physician hospital and emergency room consults	Mean y	F.E. poisson regression	0.978	0.190	0.996	0.723	na	Na
		F.E. linear regression	-0.007	0.640	-0.009	0.369	0.192	-5
	Prob. y>0	F.E. logit regression	-0.019	0.619	0.003	0.903		
Physician ambulatory consults	Mean y	F.E. poisson regression	1.034	0.049	1.073	0.000	na	Na
		F.E. linear regression	0.012	0.067	0.022	0.000	0.616	4
	Prob. y>0	F.E. logit regression	0.051	0.034	0.071	0.000		
Physician CVD related surgical procedures	Mean y	F.E. poisson regression	0.606	0.001	1.080	0.532	na	Na
		F.E. linear regression	-0.002	0.024	0.000	0.846	0.002	-6
	Prob. y>0	F.E. logit regression	0.128	0.172	-0.732	0.000		
Physician CVD related diagnostic procedures	Mean y	F.E. poisson regression	1.029	0.301	0.981	0.295	na	Na
		F.E. linear regression	0.002	0.648	-0.002	0.604	0.117	-1
	Prob. y>0	F.E. logit regression	-0.022	0.550	0.001	0.973		

Notes to tables:

- *Models for which difference-in-differences estimation is likely inappropriate are italicized.*
- *Estimates for which $p \leq 0.05$ are in bold.*
- *The shortrun estimate refers to the change in the outcome variable during the first 4 months after the introduction of RP; this change is over and above any longrun changes in the outcome variable that occur after the introduction of RP. All models estimate the effect of RP exposure after holding constant any fixed subject-specific differences in the pre-RP morbidity of the exposed and comparator groups, and any time effects on outcomes common to both groups. The parameter estimate of the F.E. (fixed effect) poisson model is the mean ratio of the number of events observed after exposure to RP (in either the short run or long run) relative to the number of events observed for those not exposed. The parameter estimates of the F.E. (fixed effect) linear regression model is the mean change in the number of events observed after exposure to RP relative to the number of events observed for those non-exposed. The parameter estimates of the F.E. (fixed effect) logit regression model indicate the log of the odds of an event conditional on exposure to RP relative to the odds of an event conditional on non-exposure. The exponential transformation of the log odds ratio produces the odds ratio – this indicates the odds of an event conditional on exposure to RP relative to the odds of an event conditional on non-exposure. If the log odds ratio is close to 0, then the numbers after the decimal approximates the increase in the odds of the event for the exposed group relative to the odds of the event for the non-exposed group. Example: if log odds = 0.12, then $\exp(0.12) = 1.127$, meaning that the odds of an event are 13% higher for the exposed relative to the non exposed.*

Figure 33 Mean number of ambulatory physician consultations, by Nitrates RP exposure status, and month

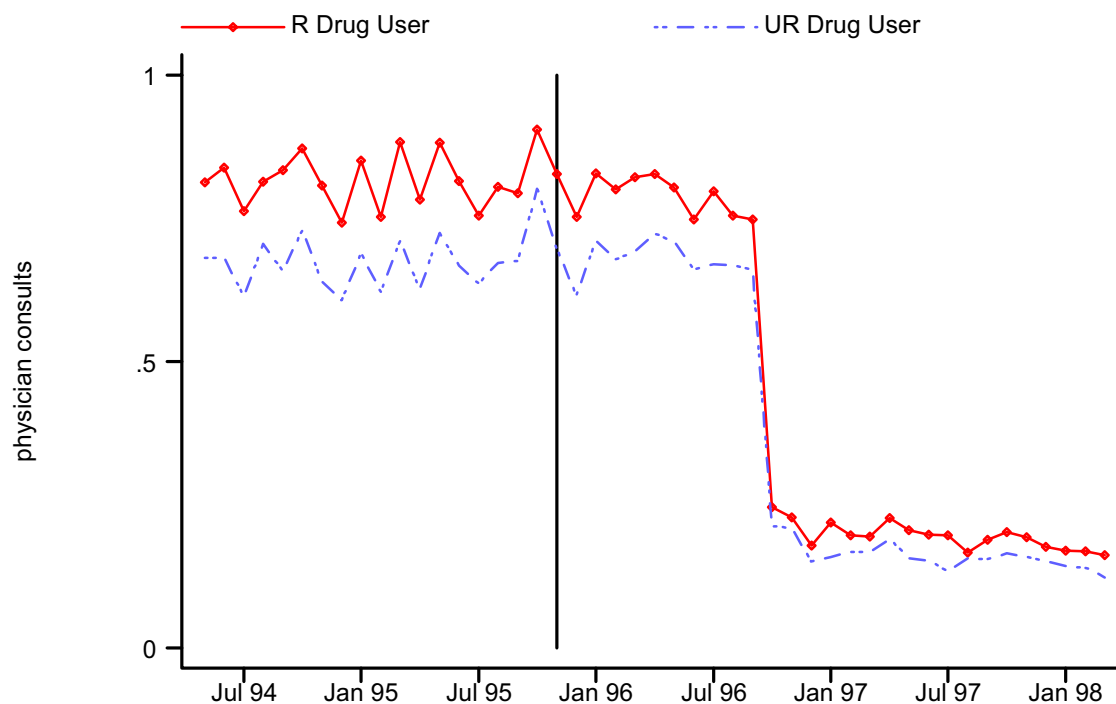


Figure 34 Probability of ambulatory physician consultation, by Nitrates RP exposure status, and month

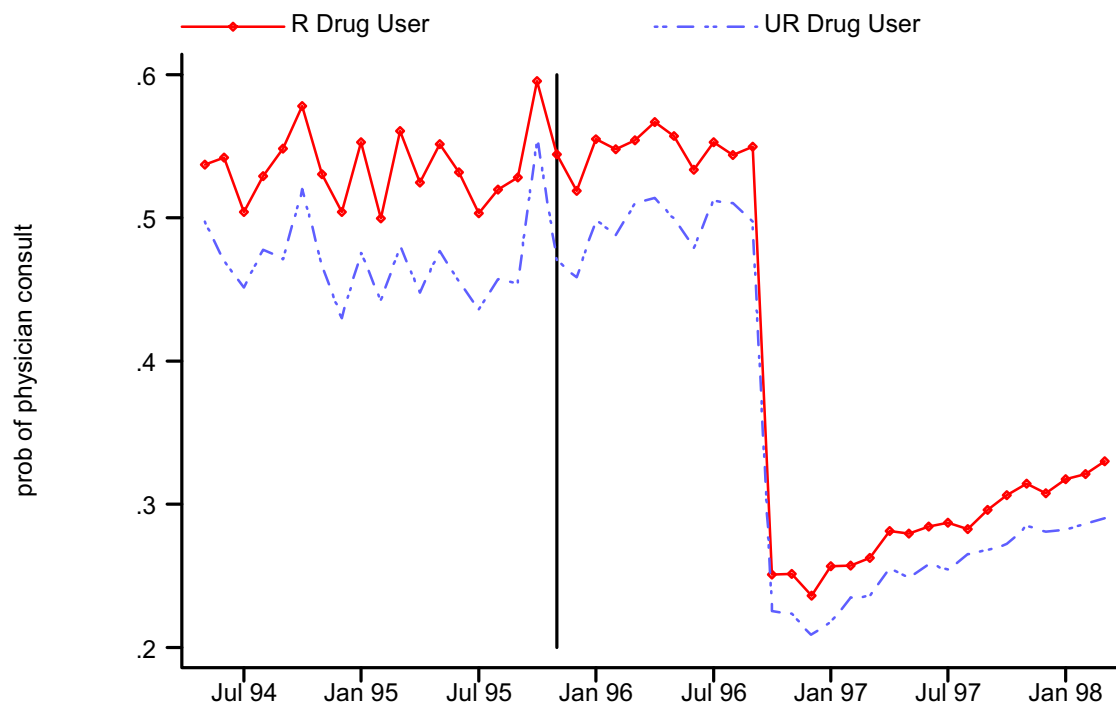


Figure 35 Mean number of physician ER/hospital visits, by Nitrates RP exposure status, and month

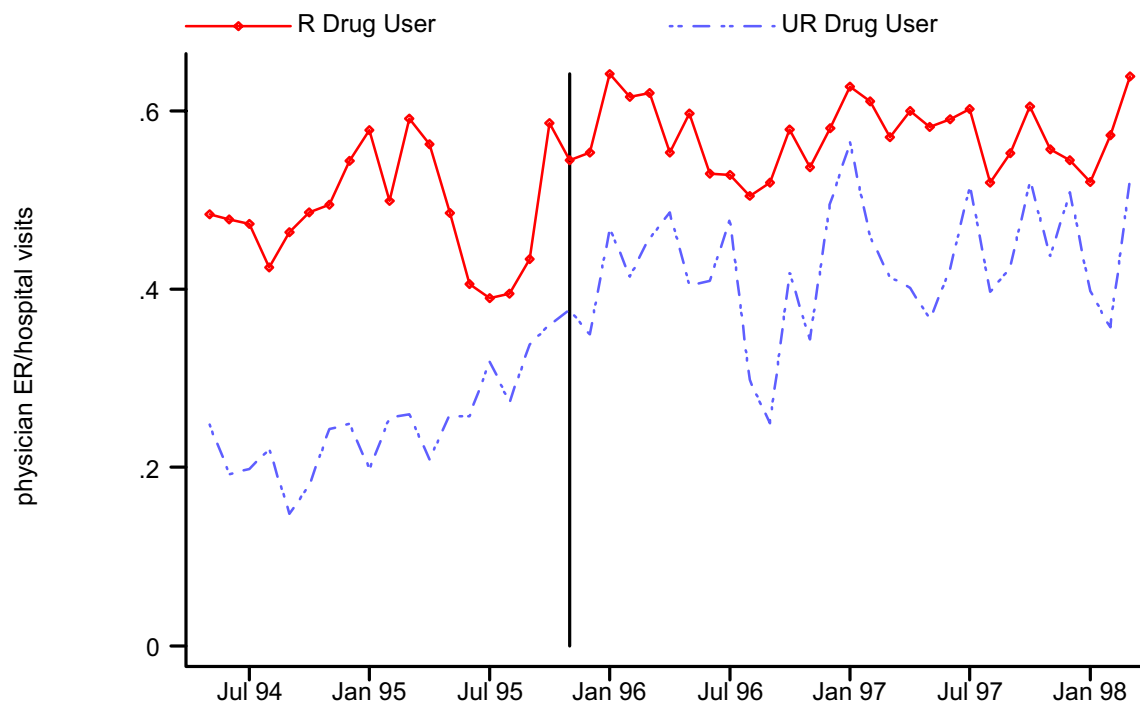


Figure 36 Probability of physician ER/hospital visit, by Nitrates RP exposure status, and month

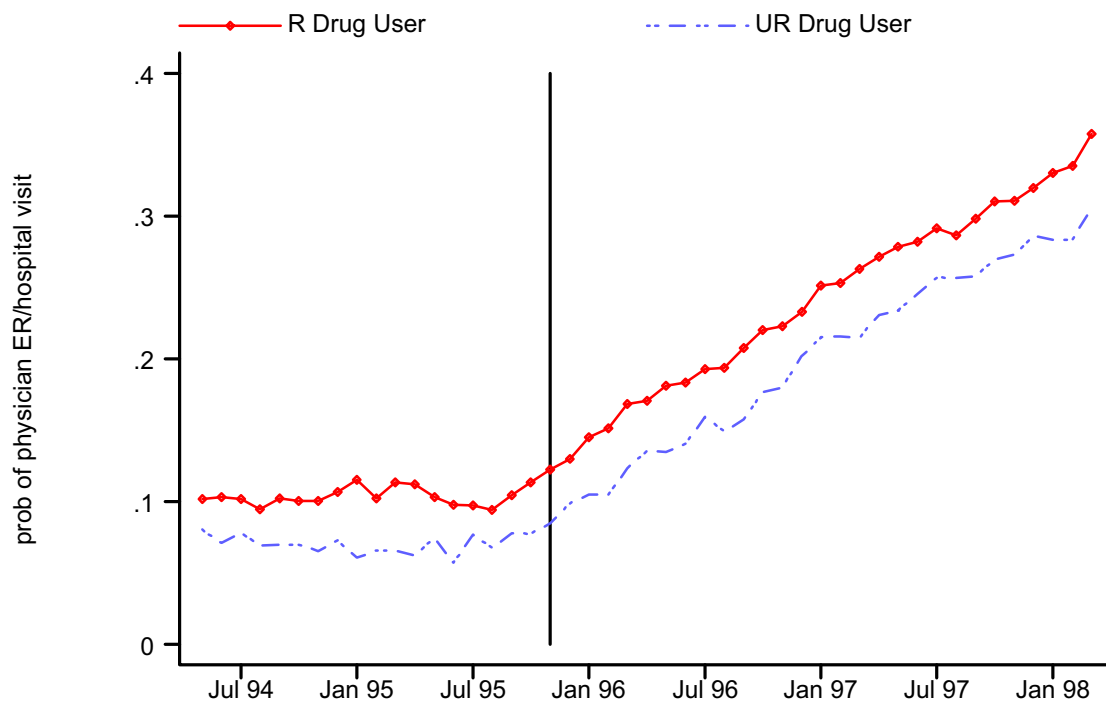


Figure 37 Mean number of physician CVD diagnostic procedures, by Nitrates RP exposure status, and month

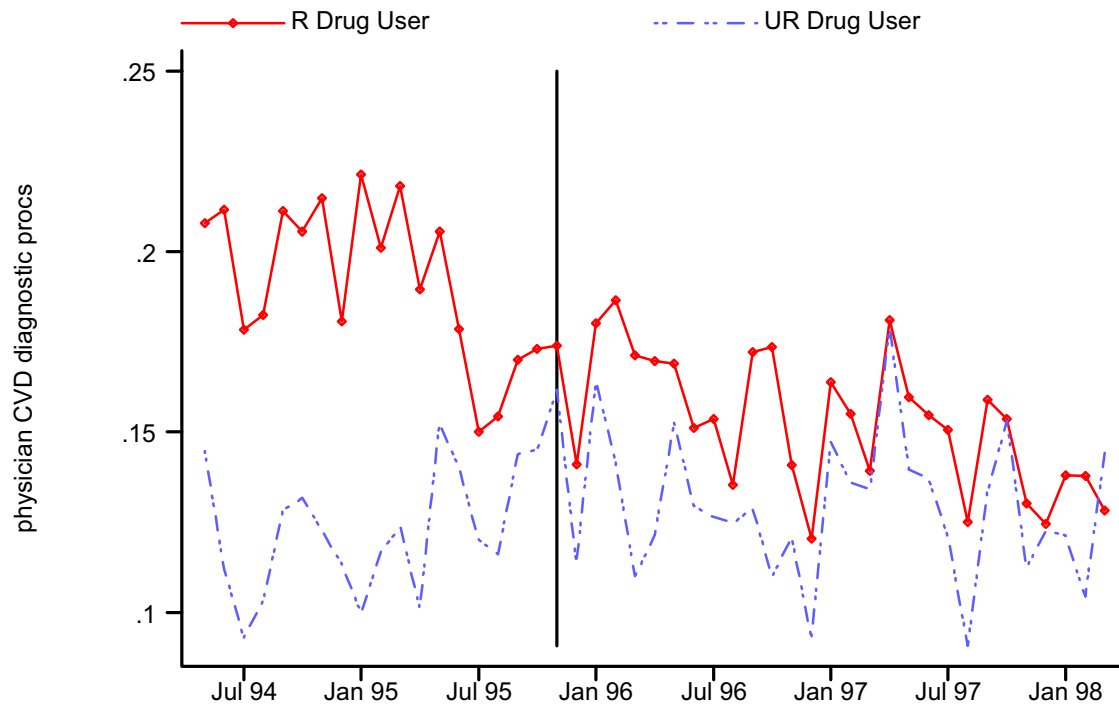


Figure 38 Probability of physician CVD diagnostic procedures, by Nitrates RP exposure status, and month

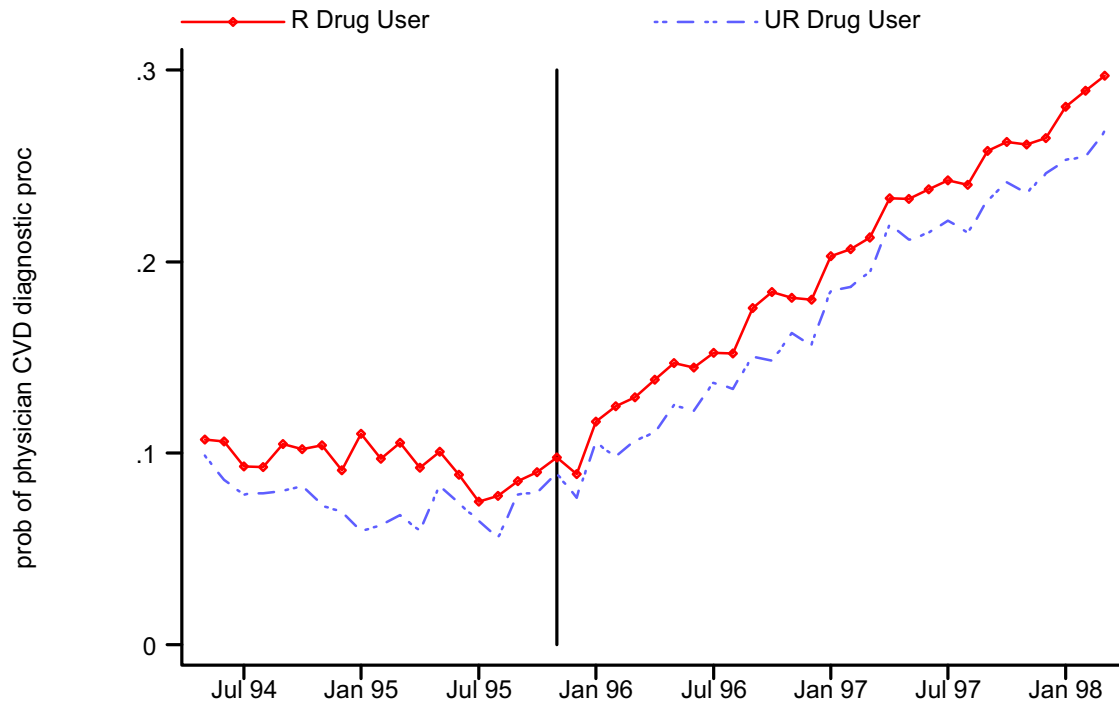


Figure 39 Mean number of physician CVD surgical procedures, by Nitrates RP exposure status, and month

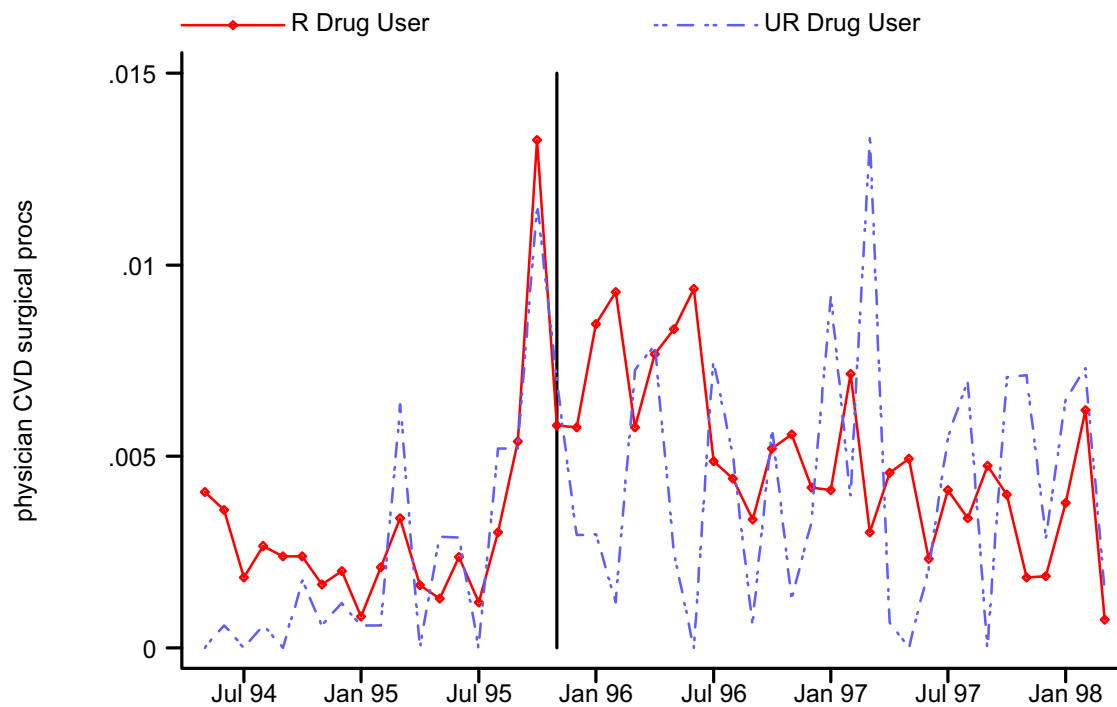


Figure 40 Probability of physician CVD surgical procedure, by Nitrates RP exposure status, and month

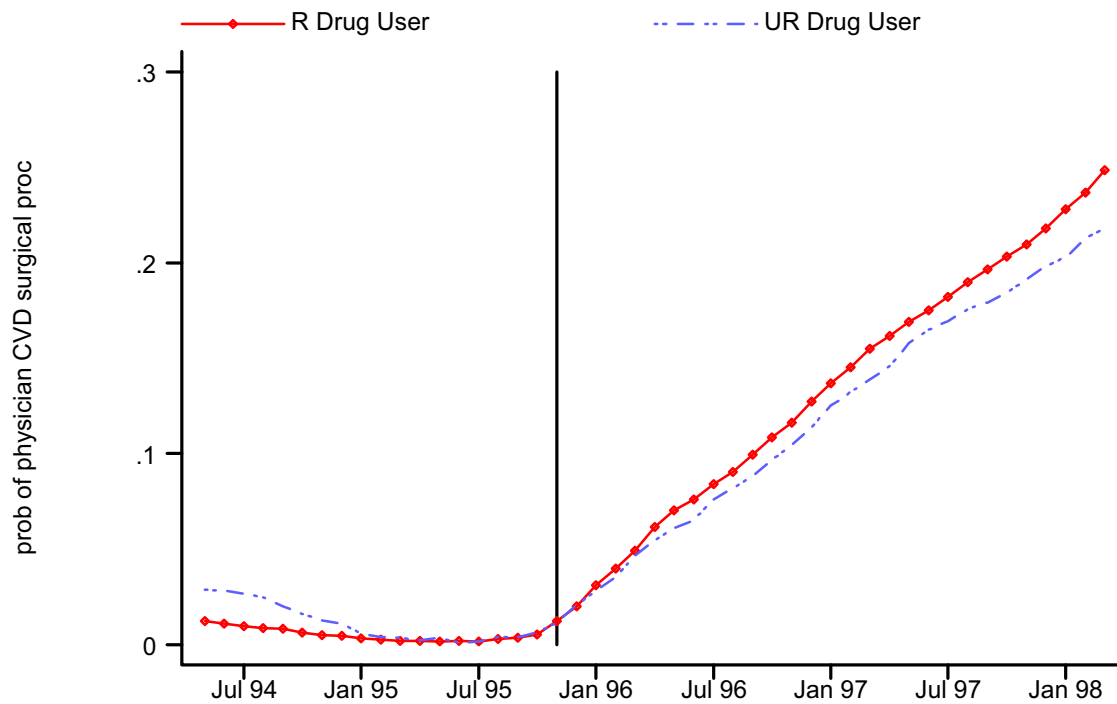


Figure 41 Mean number of hospital admission for cardiovascular or renal conditions, by Nitrates RP exposure status, and month

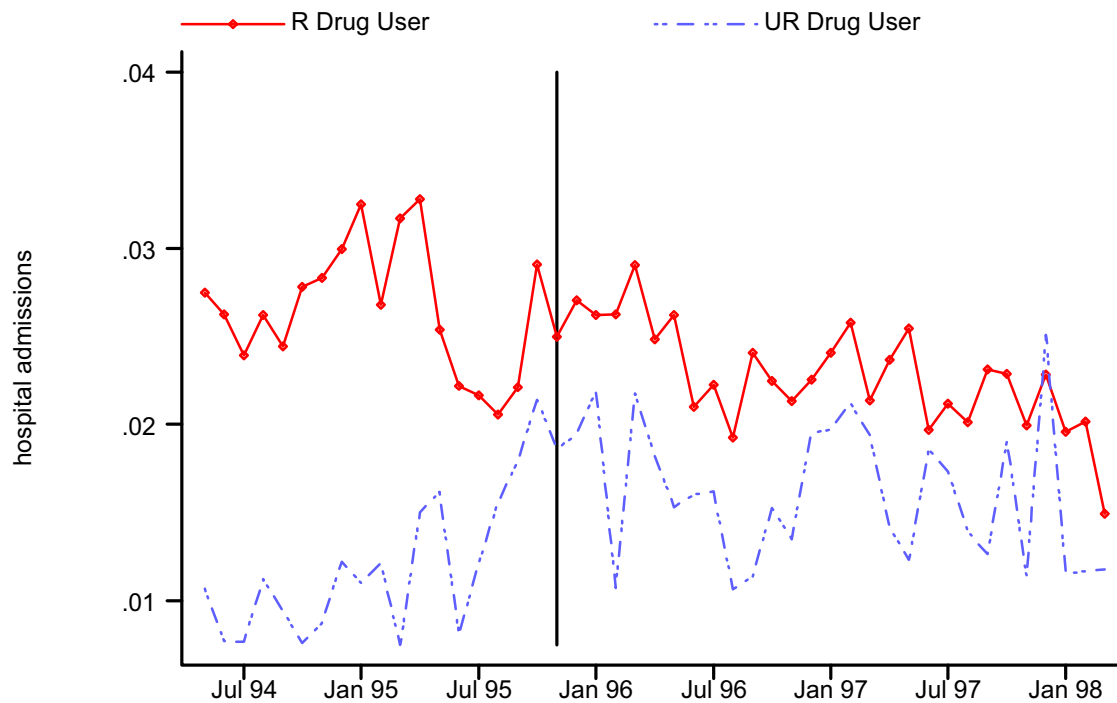


Figure 42 Probability of hospital admission for cardiovascular or renal condition, by Nitrates RP exposure status, and month

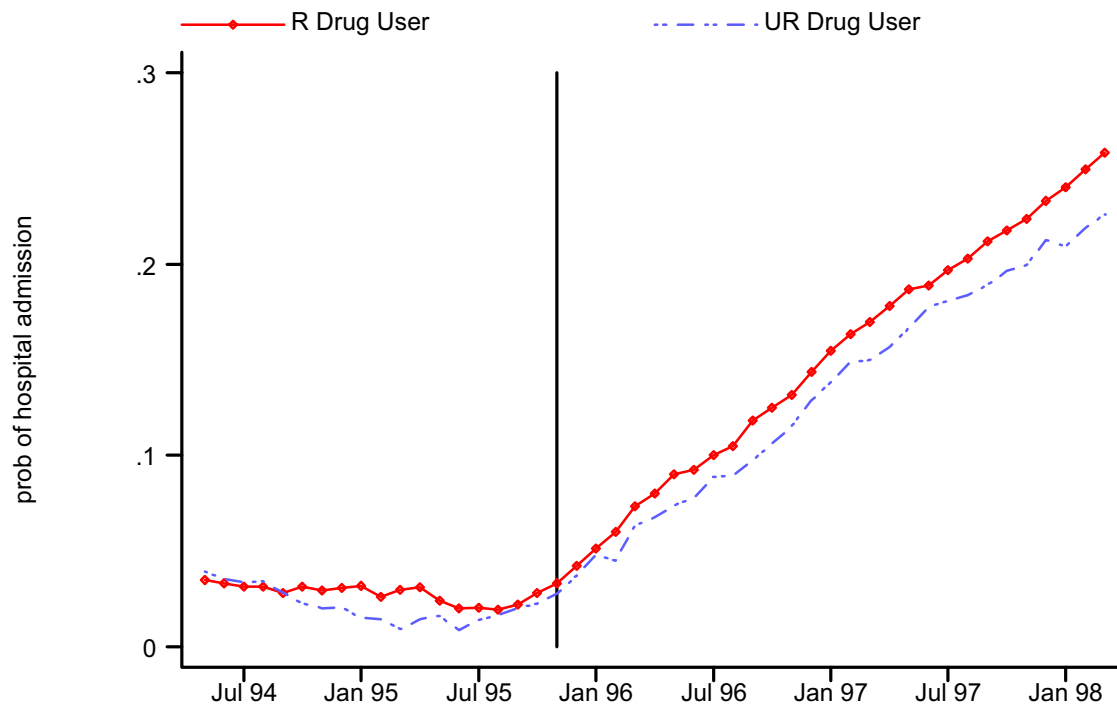


Figure 43 Mean number of days in hospital for cardiovascular or renal condition, by Nitrates RP exposure status, and month

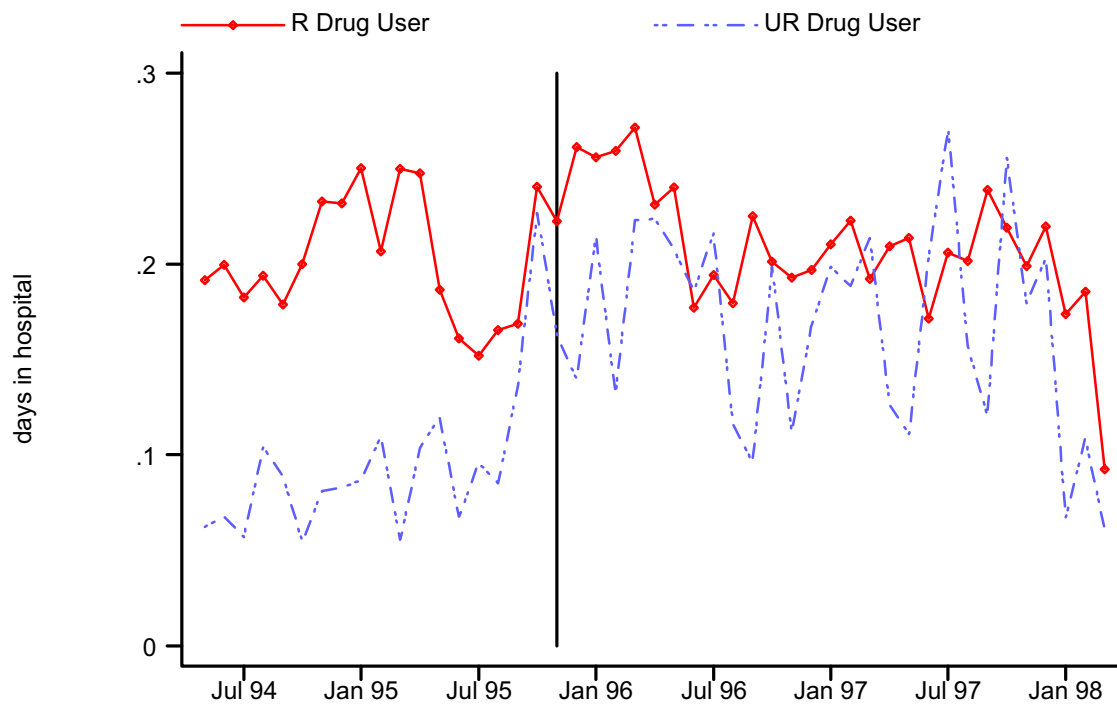


Figure 44 Probability of day in hospital for cardiovascular or renal condition, by Nitrates RP exposure status, and month

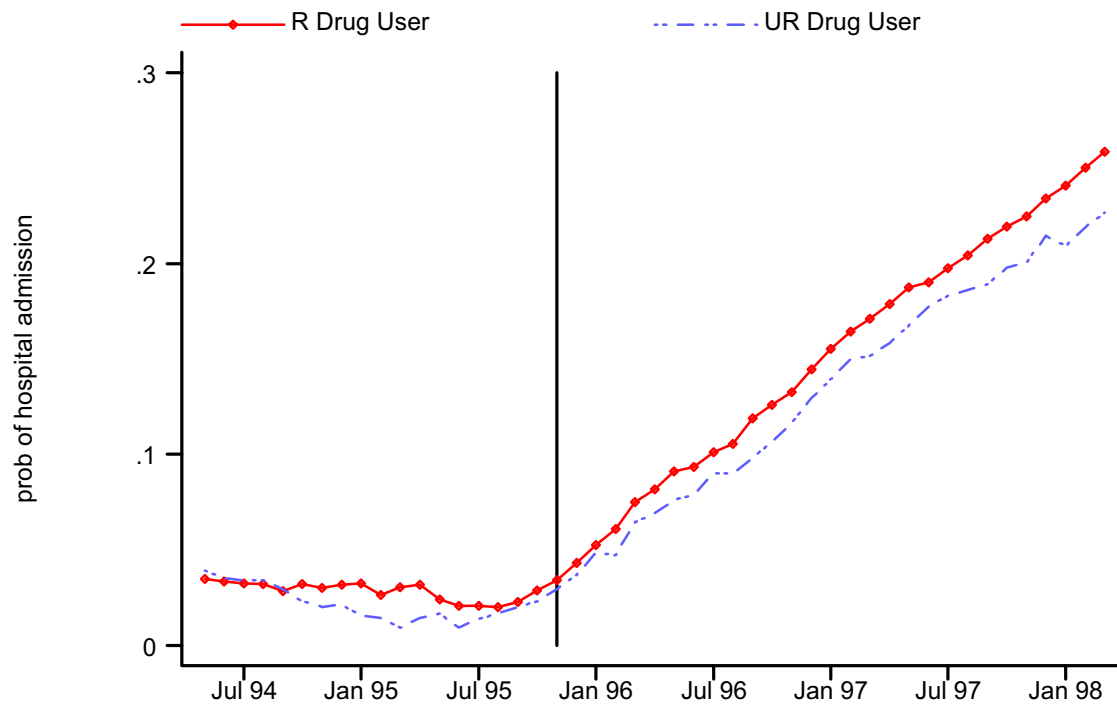


Figure 45 Mean number of revascularizations, by Nitrates RP exposure status, and month

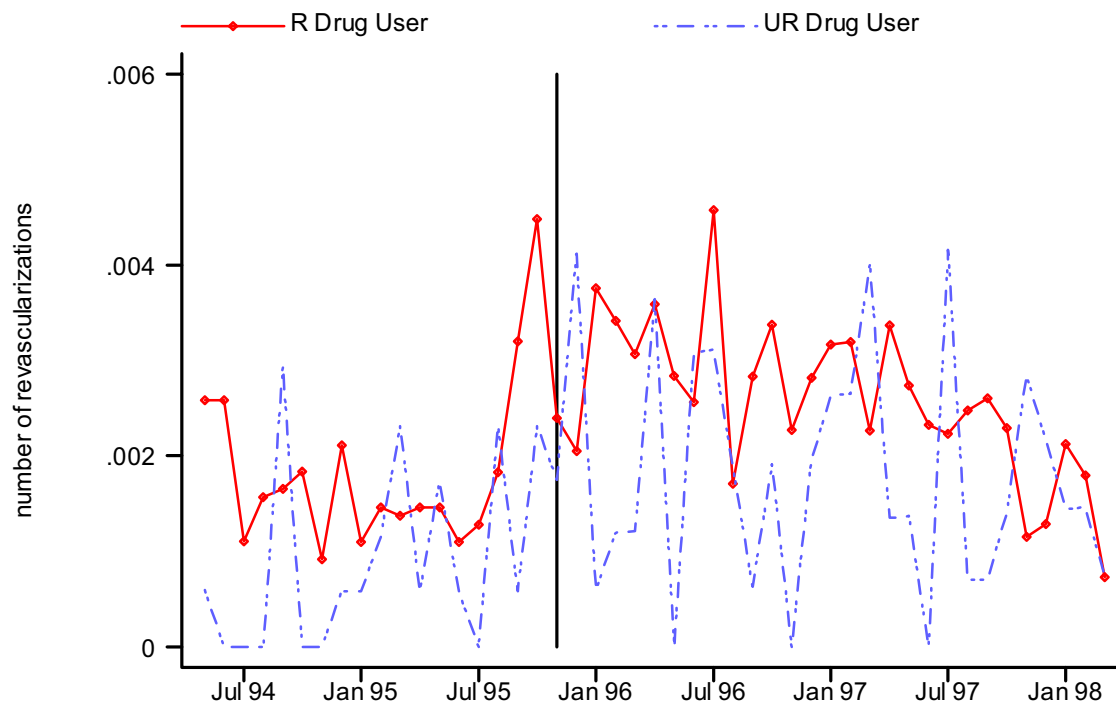


Figure 46 Probability of revascularization, by Nitrates RP exposure status, and month

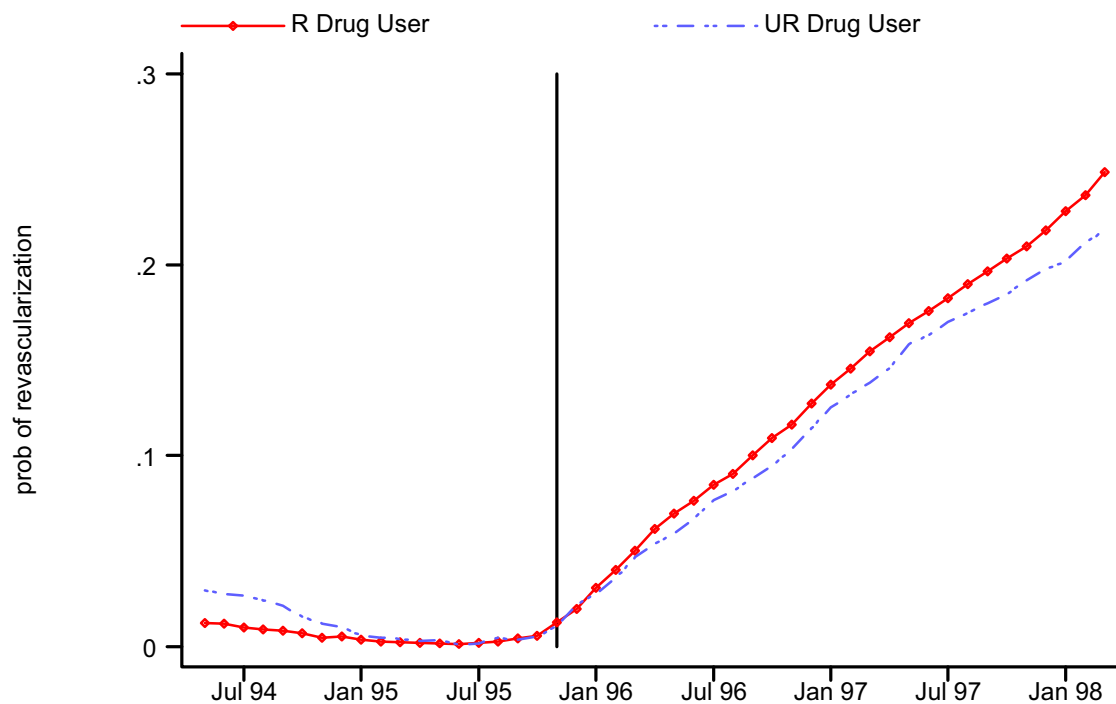


Figure 47 Mean number of prescriptions for sublingual nitroglycerin, by Nitrates RP exposure status, and month

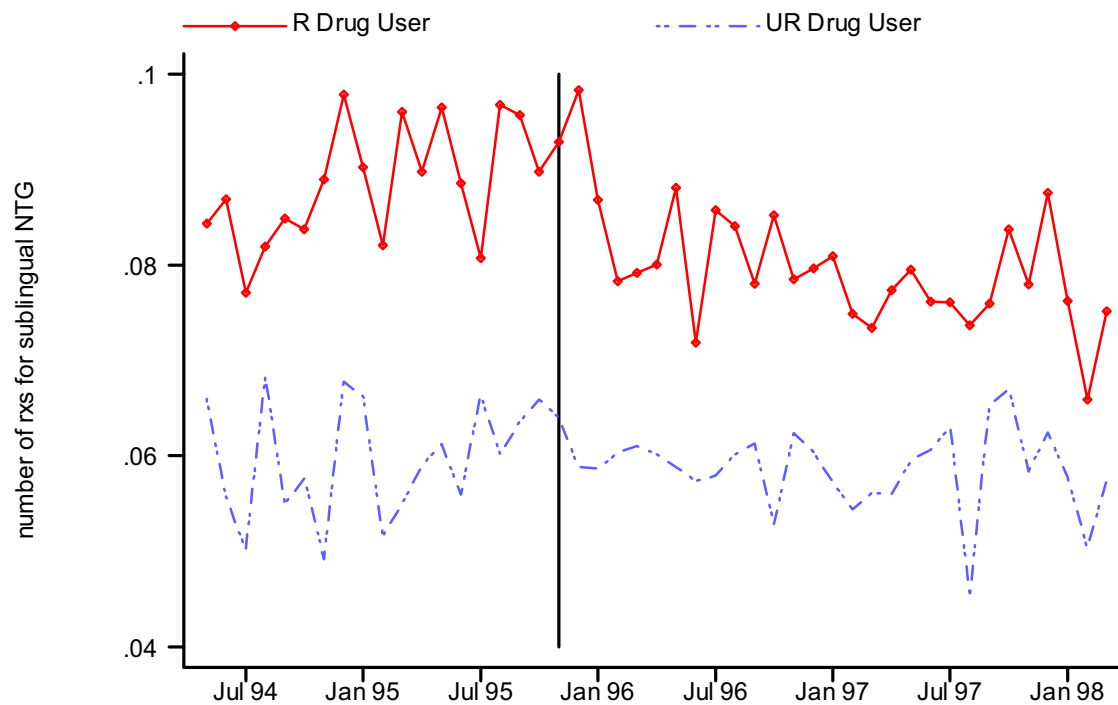


Figure 48 Probability of prescription for sublingual nitroglycerin, by Nitrates RP exposure status, and month

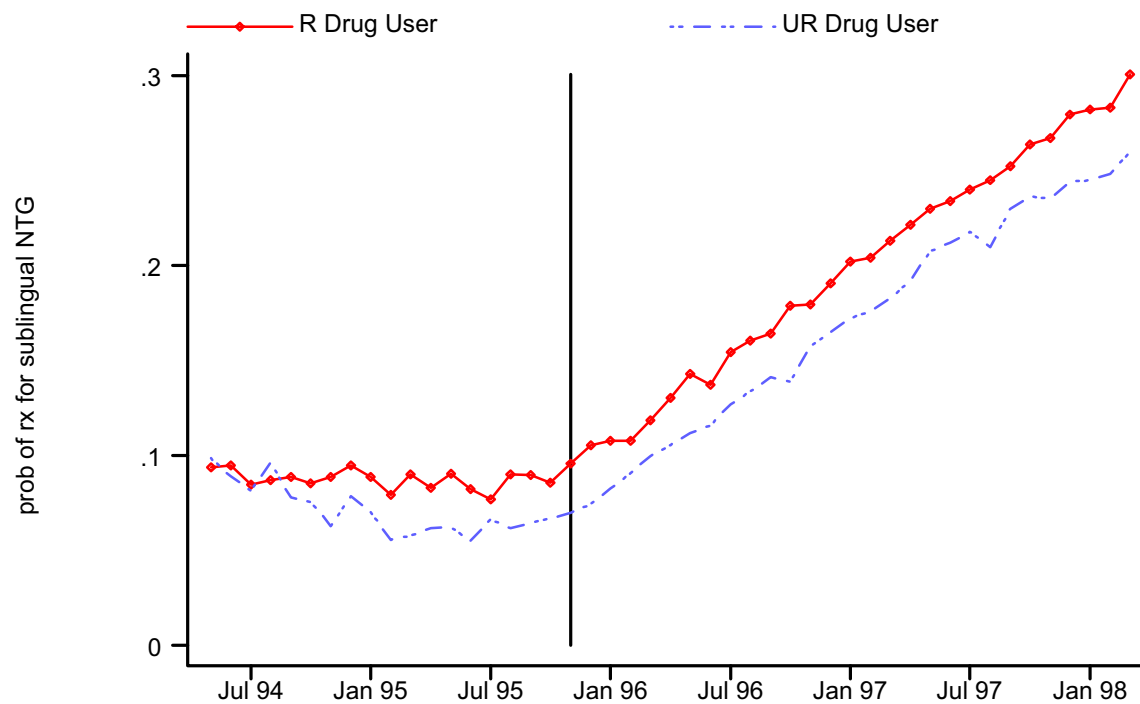


Figure 49 Mean number of physician consultations, by ACE inhibitor RP exposure status, and month

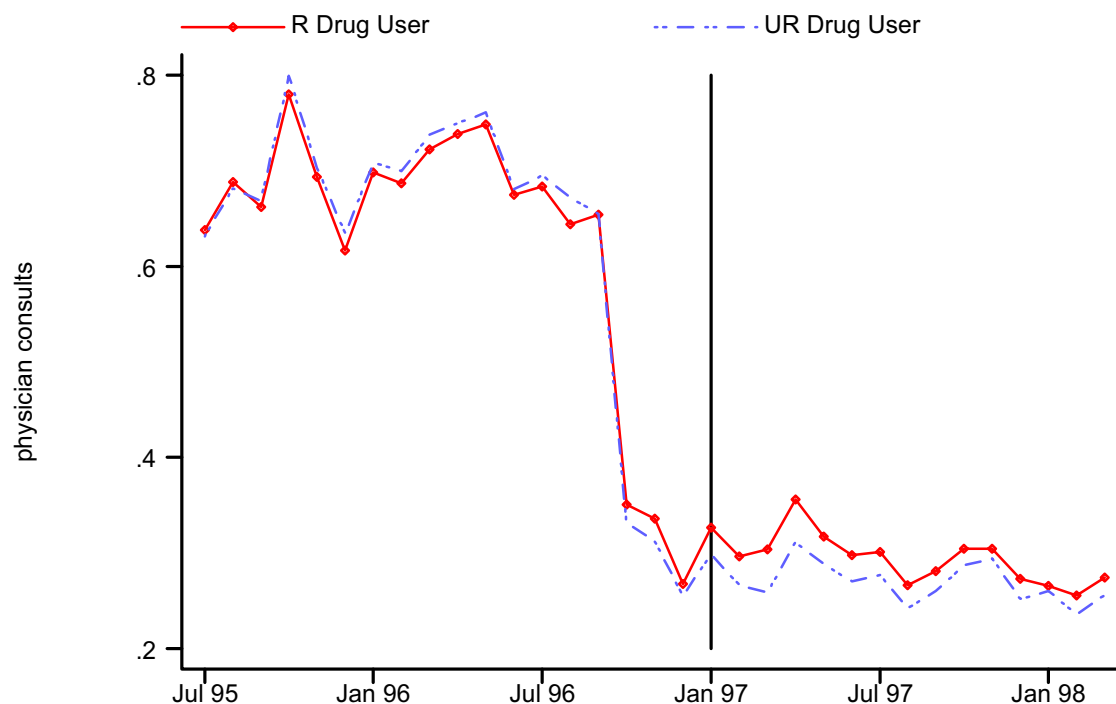


Figure 50 Probability of physician consultation, by ACE inhibitor RP exposure status, and month

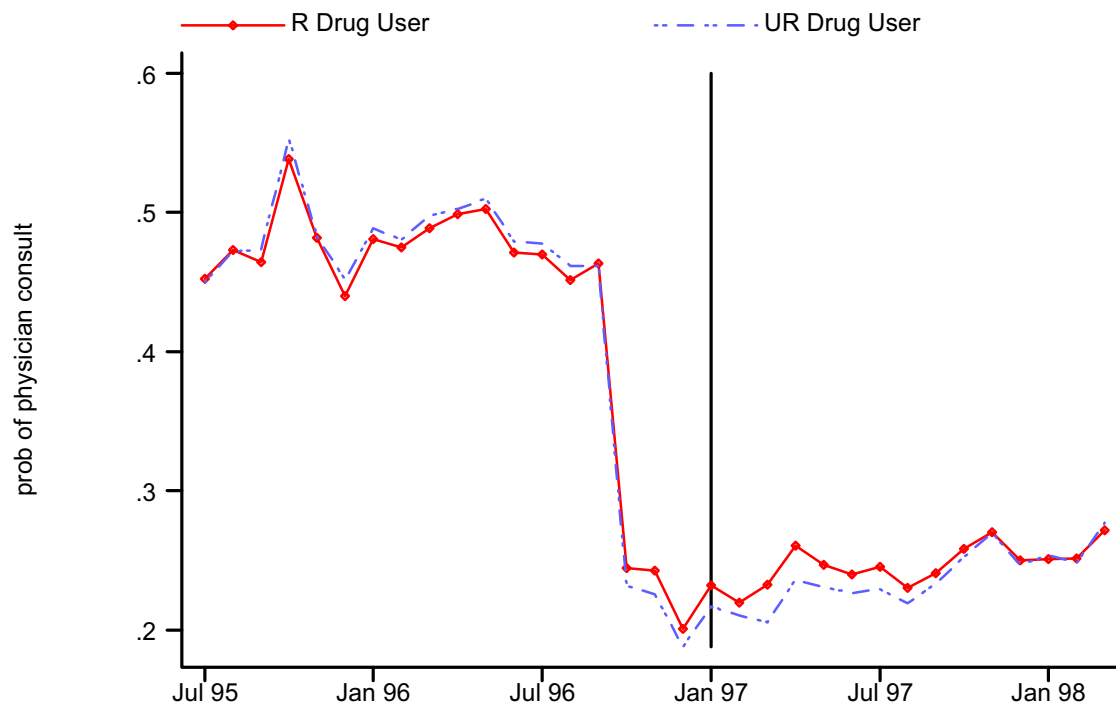


Figure 51 Mean number of physician ER/hospital visits, by ACE inhibitor RP exposure status, and month

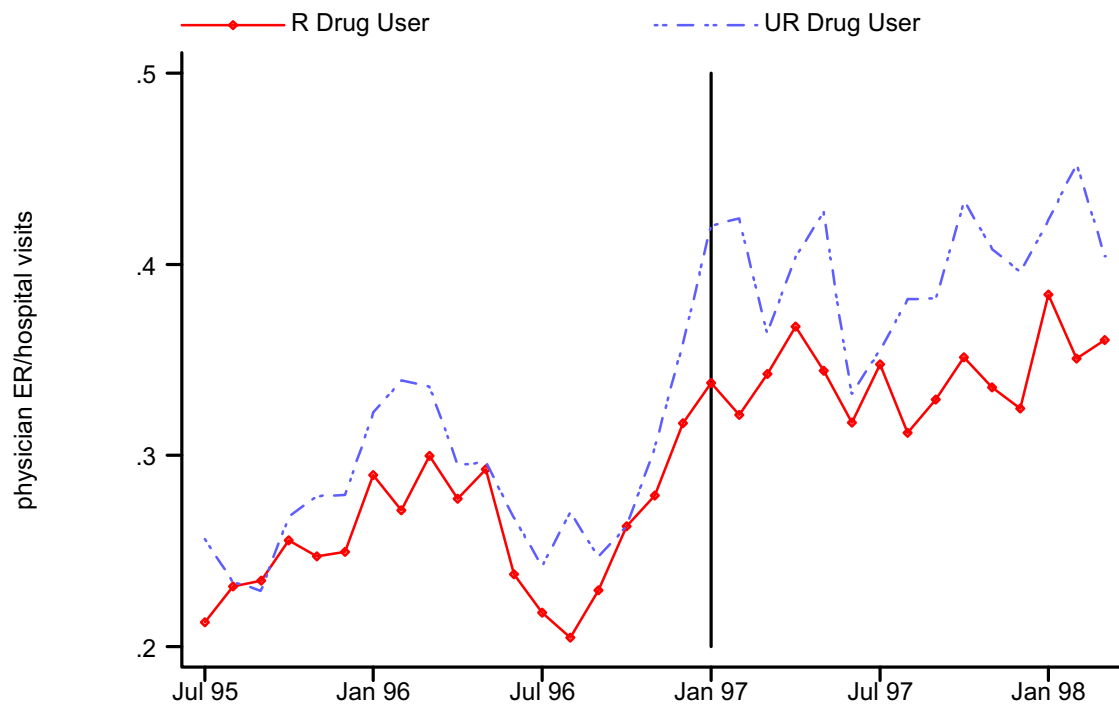


Figure 52 Probability of physician ER/hospital visit, by ACE inhibitor RP exposure status, and month

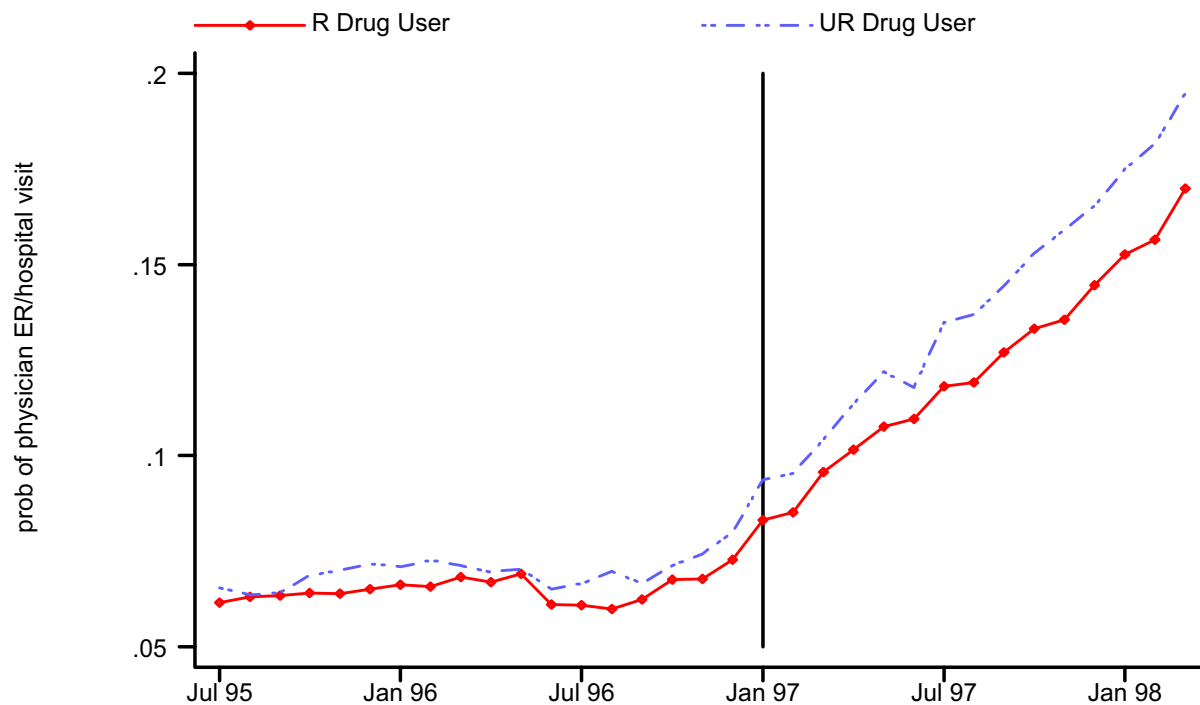


Figure 53 Mean number of physician CVD diagnostic procedures, by ACE inhibitor RP exposure status, and month

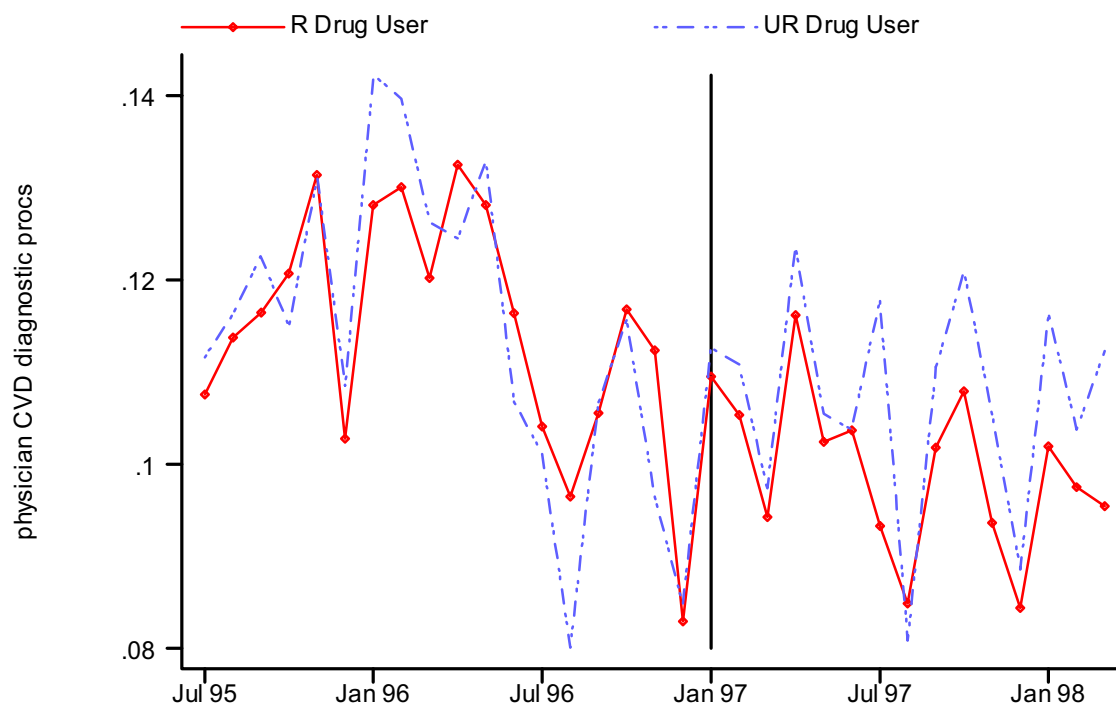


Figure 54 Probability of physician CVD diagnostic procedure, by ACE inhibitor RP exposure status, and month

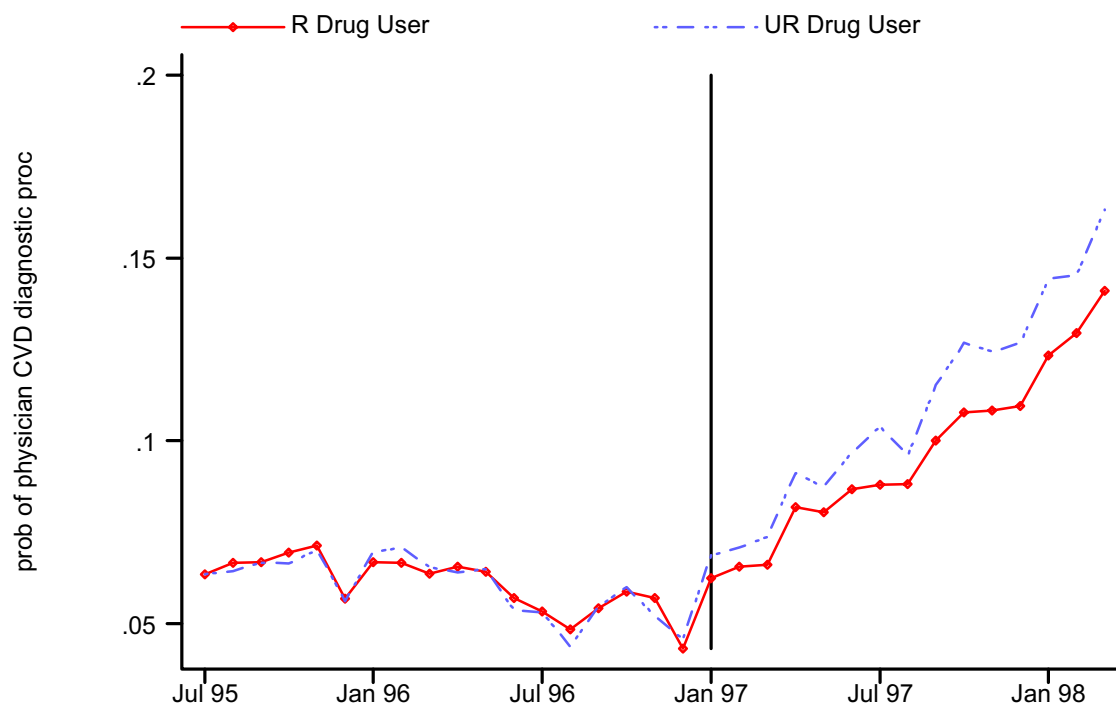


Figure 55 Mean number of physician CVD surgical procedures, by ACE inhibitor RP exposure status, and month

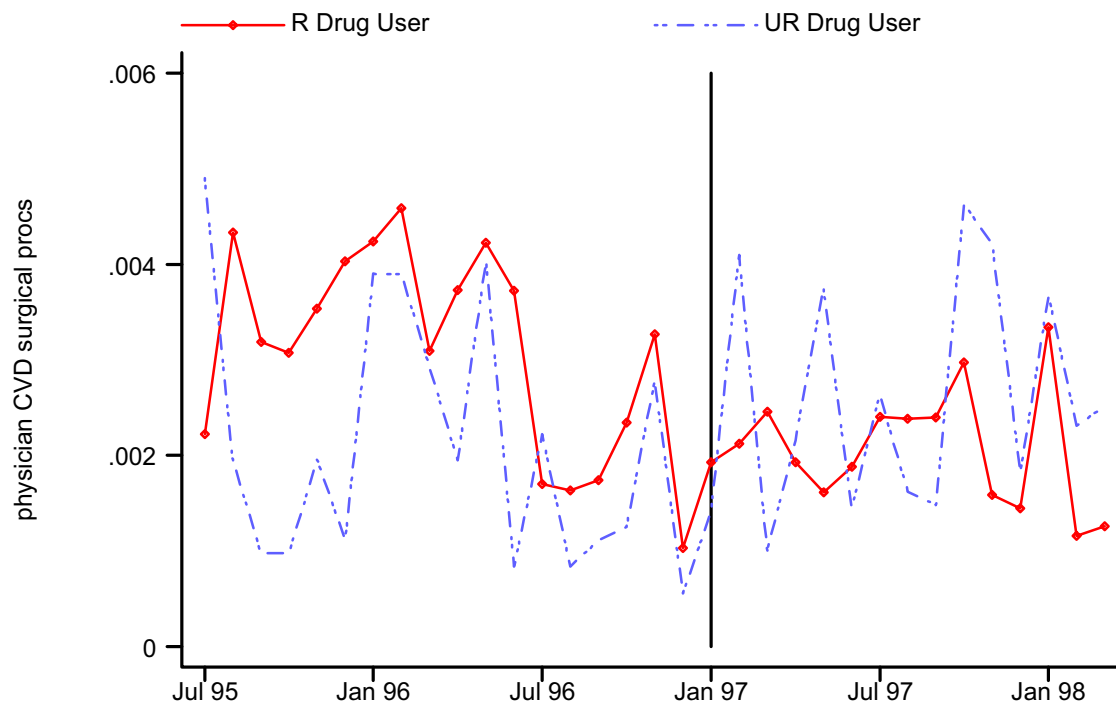


Figure 56 Probability of physician CVD surgical procedure, by ACE inhibitor RP exposure status, and month

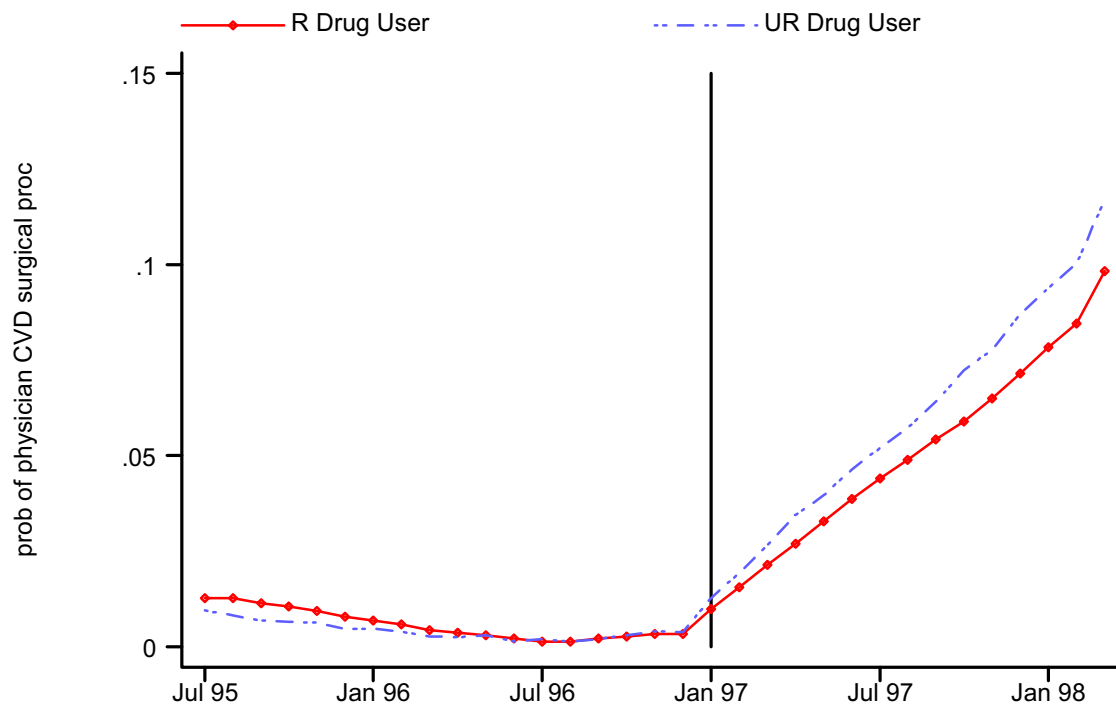


Figure 57 Mean number of hospital admissions for cardiovascular or renal conditions, by ACE inhibitor RP exposure status, and month

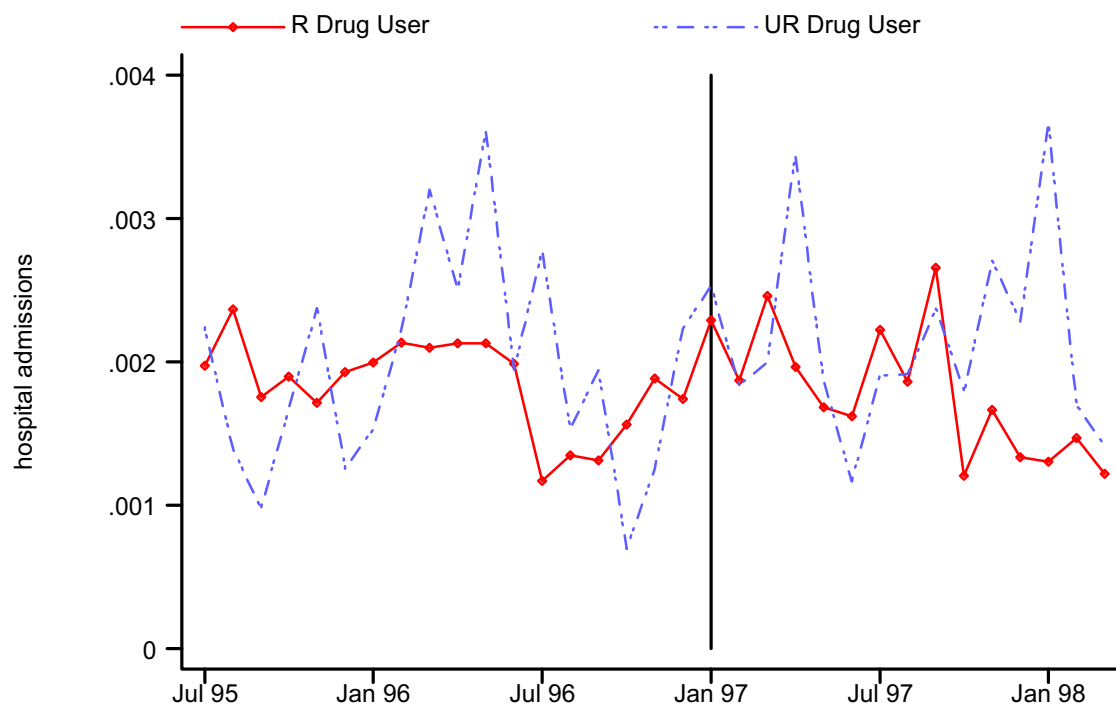


Figure 58 Probability of hospital admission for cardiovascular or renal condition, by ACE inhibitor RP exposure status, and month

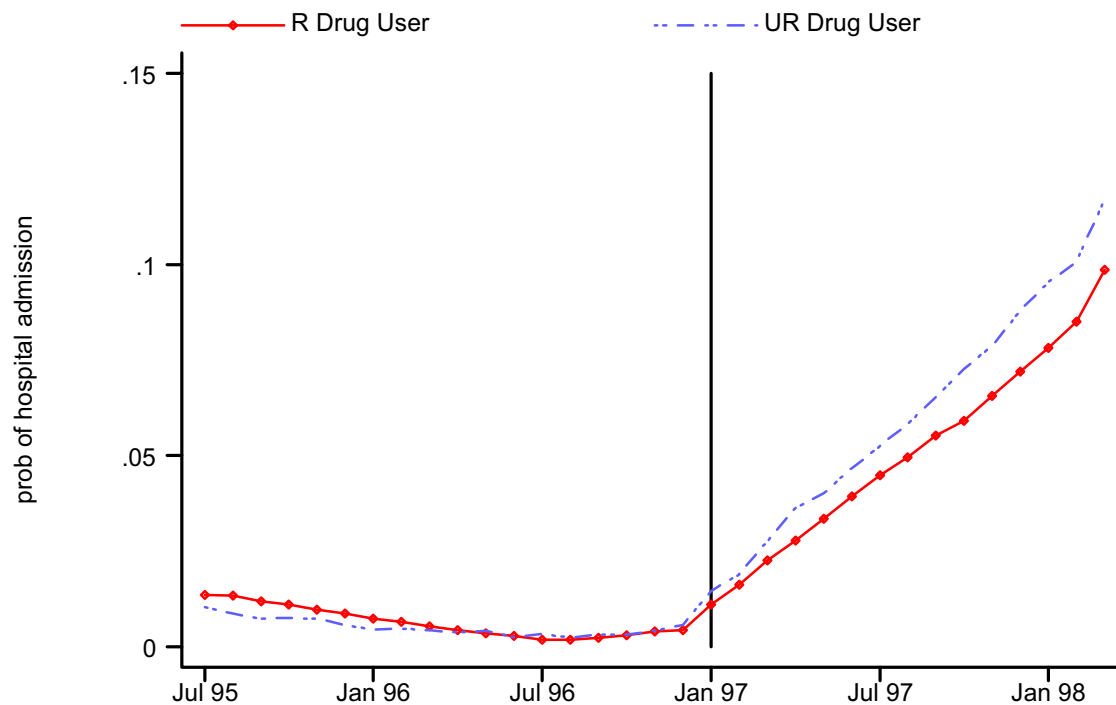


Figure 59 Mean number of days in hospital for cardiovascular or renal condition, by ACE inhibitor RP exposure status, and month

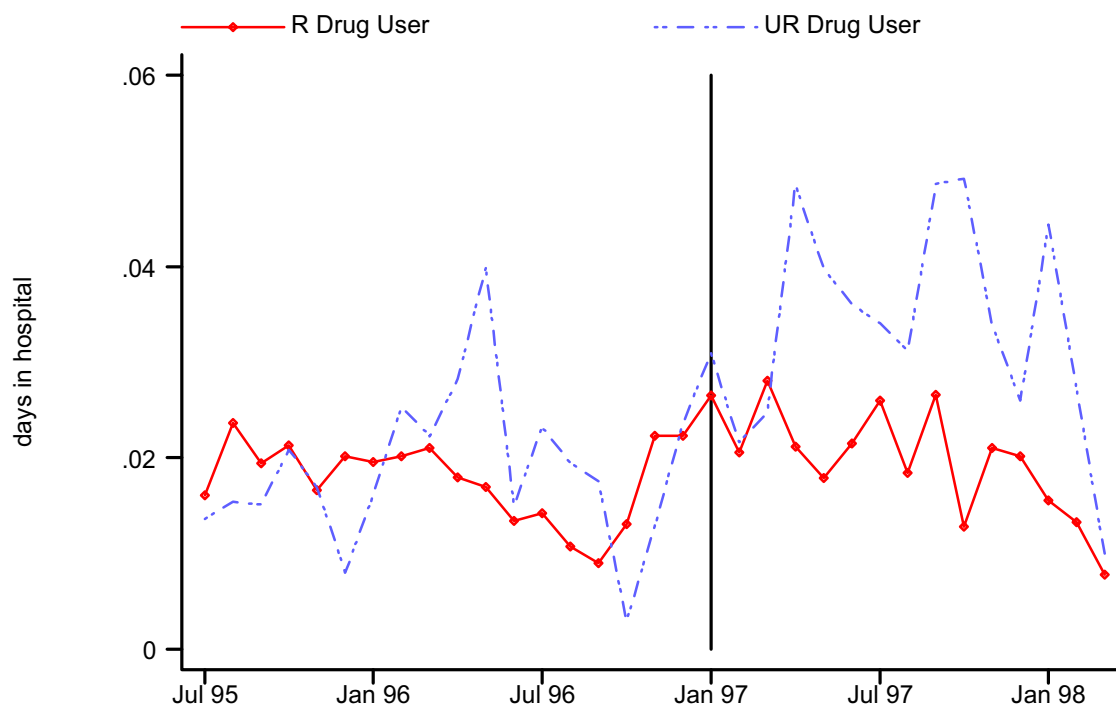


Figure 60 Probability of day in hospital for cardiovascular or renal condition, by ACE inhibitor RP exposure status, and month

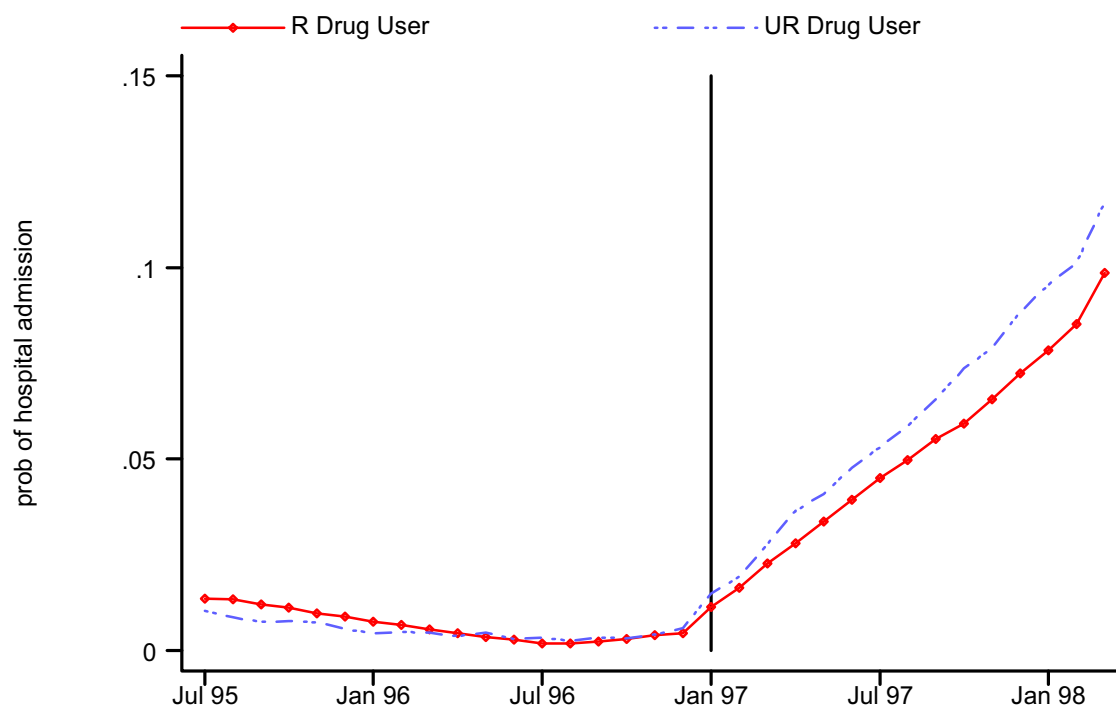


Figure 61 Mean number of revascularizations, by ACE inhibitor RP exposure status, and month

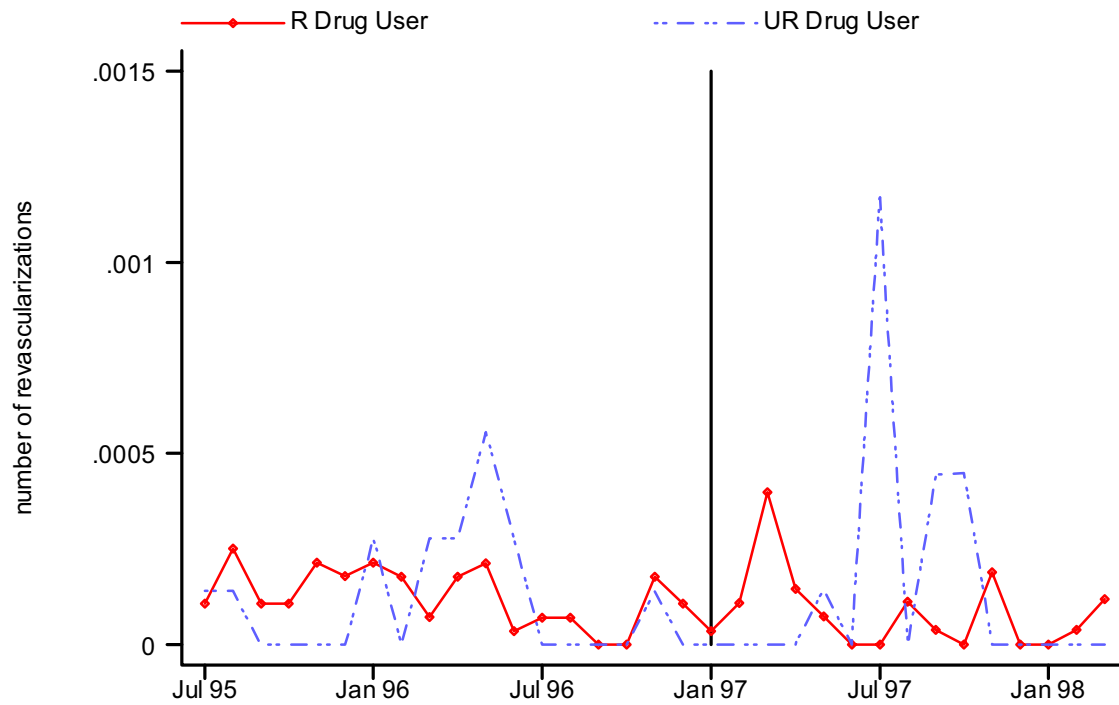


Figure 62 Probability of revascularization, by ACE inhibitor RP exposure status, and month

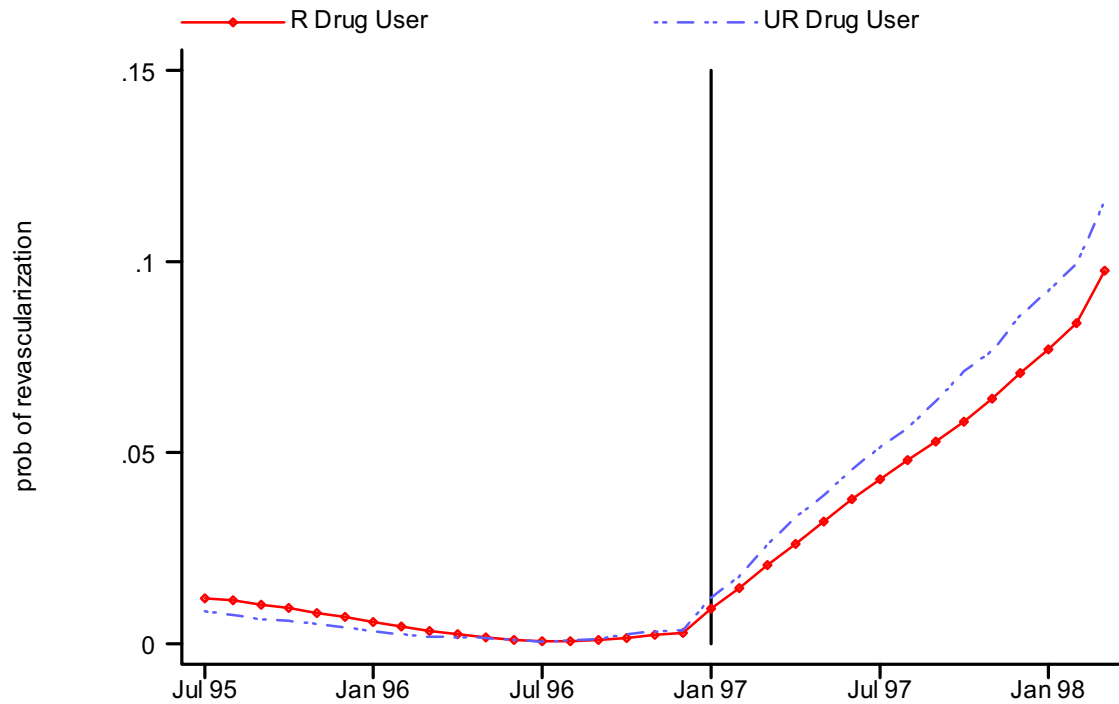


Figure 63 Mean number of prescriptions for sublingual nitroglycerin, by ACE inhibitor RP exposure status, and month

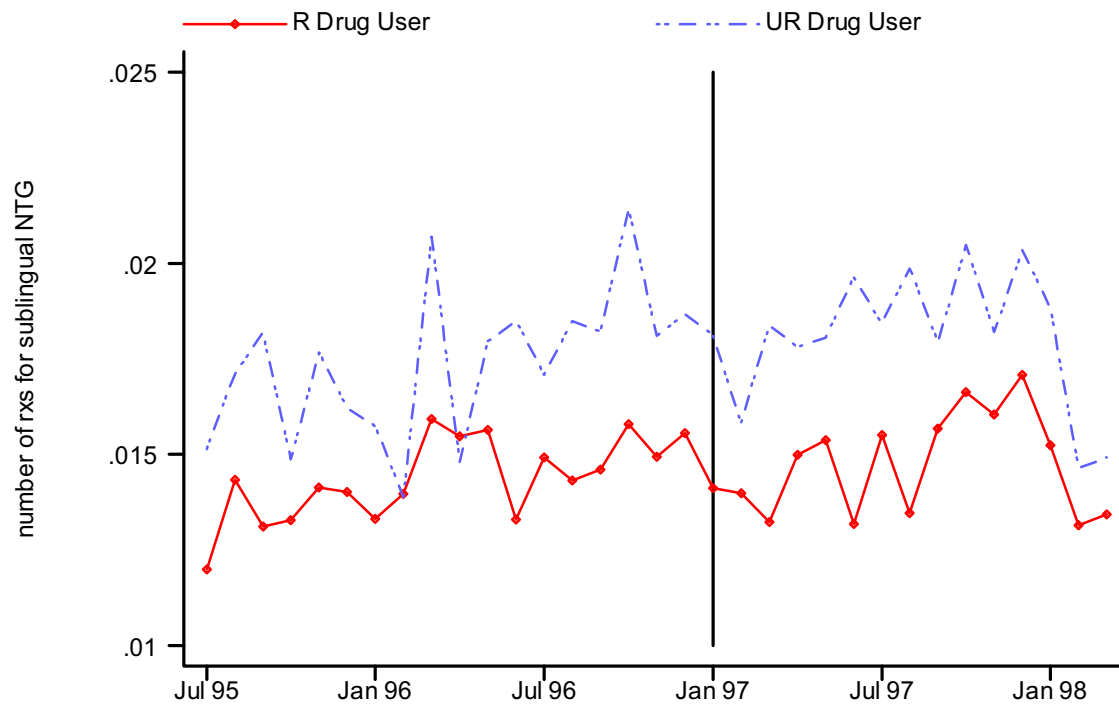


Figure 64 Probability of prescription for sublingual nitroglycerin, by ACE inhibitor RP exposure status, and month

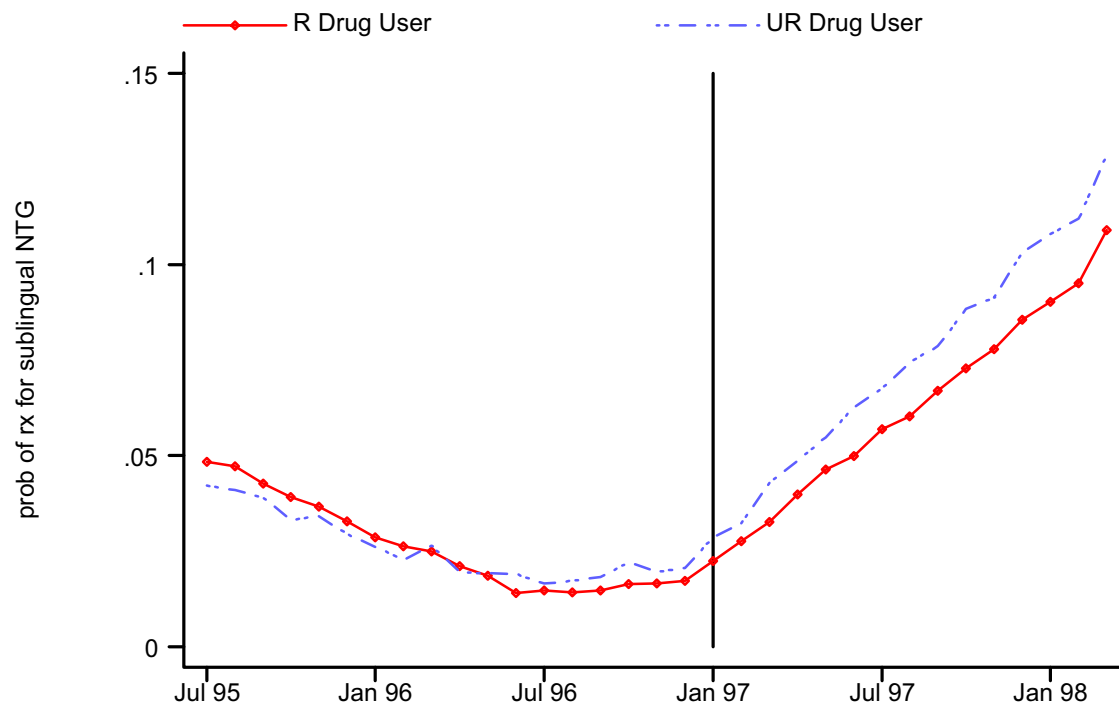


Figure 65 Mean number of physician consultations, by CCBs RP exposure status, and month

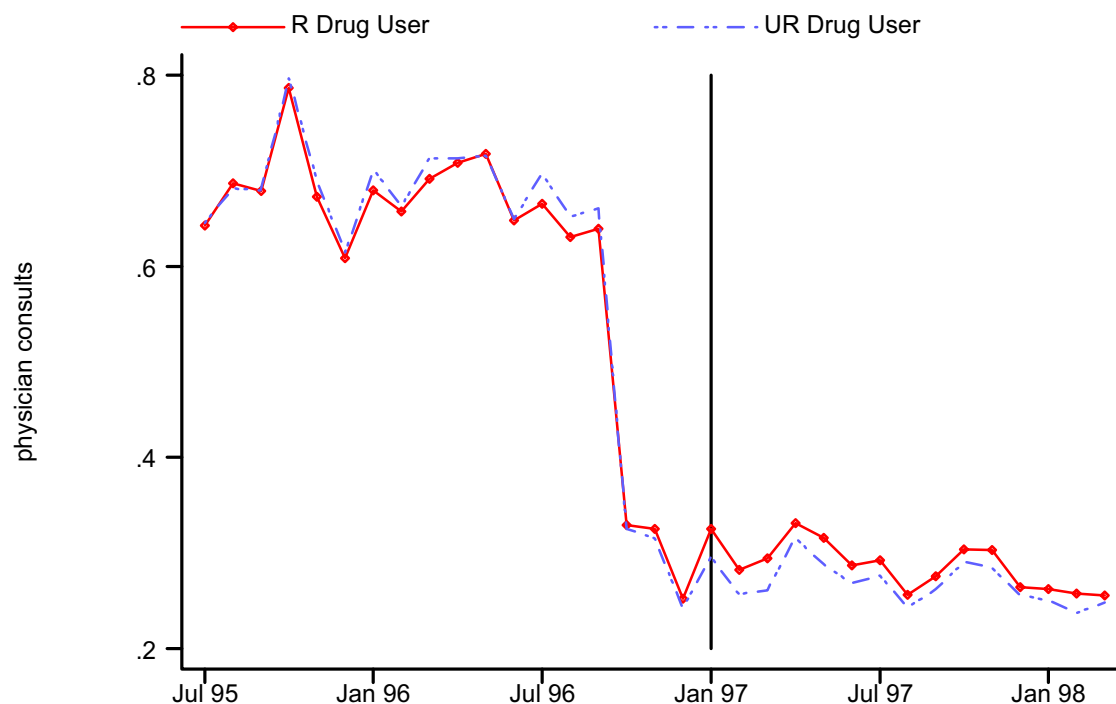


Figure 66 Probability of physician consultation, by CCBs RP exposure status, and month

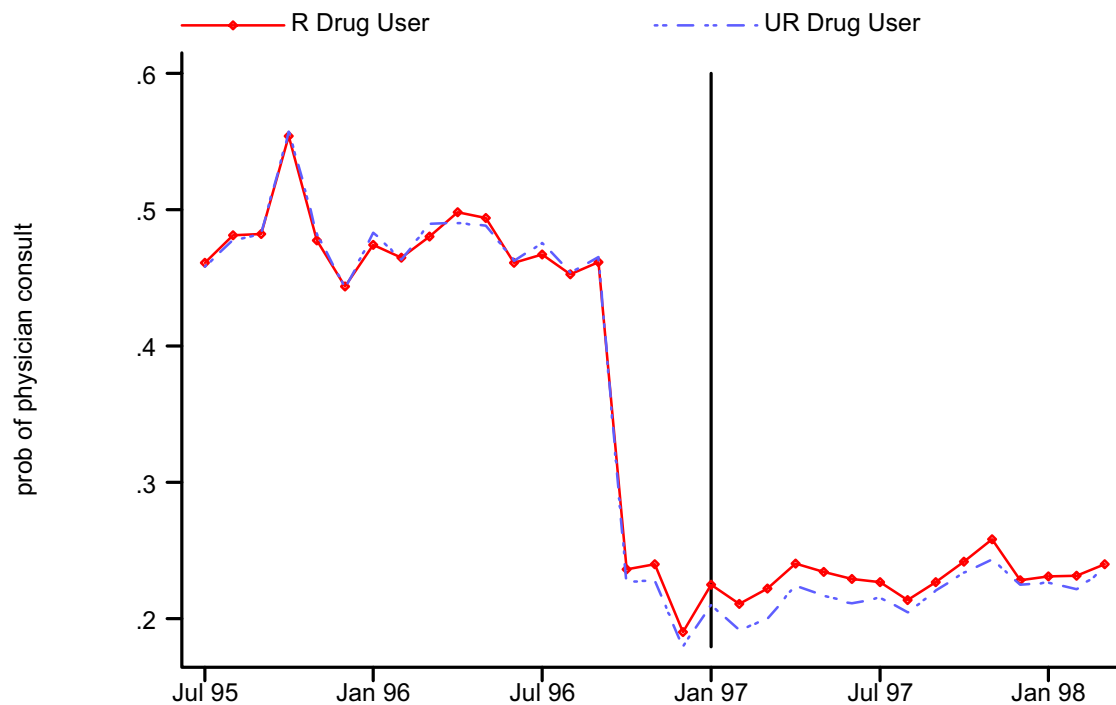


Figure 67 Mean number of physician ER/hospital visits, by CCBs RP exposure status, and month

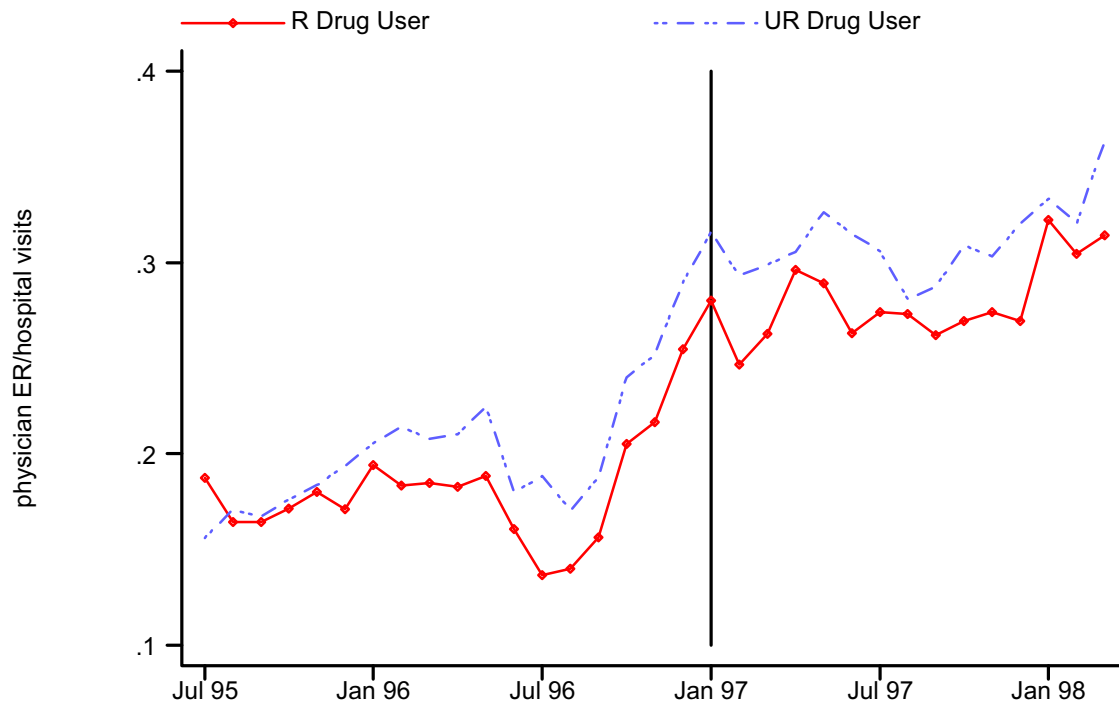


Figure 68 Probability of physician ER/hospital visit, by CCBs RP exposure status, and month

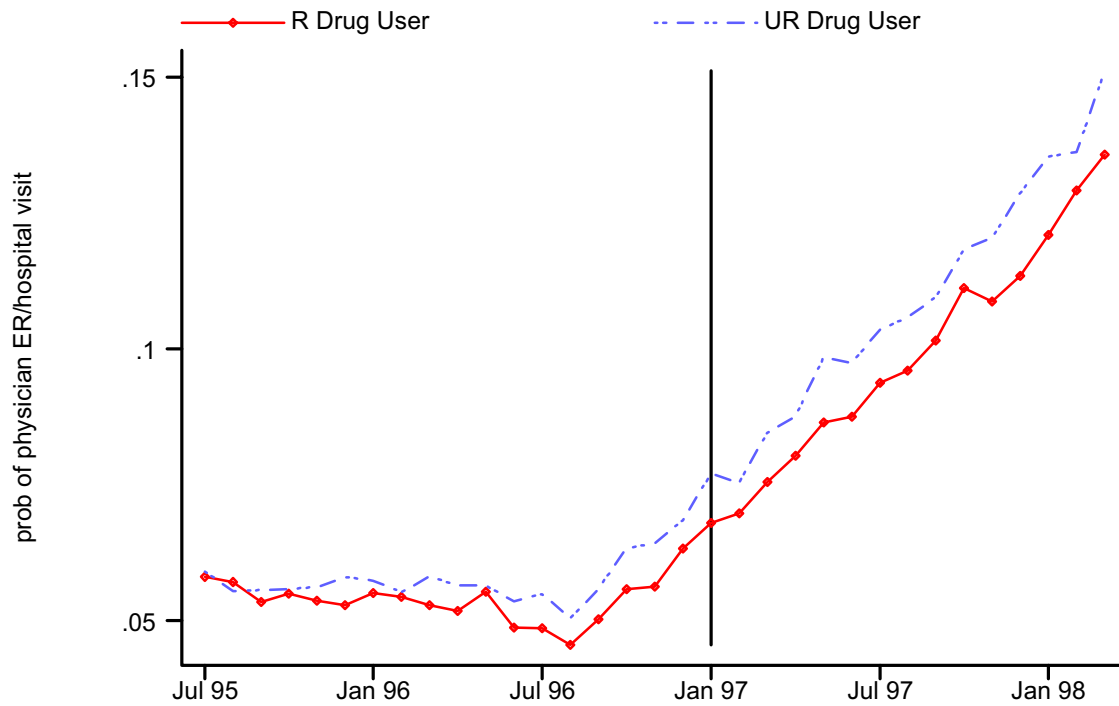


Figure 69 Mean number of physician CVD diagnostic procedures, by CCBs RP exposure status, and month

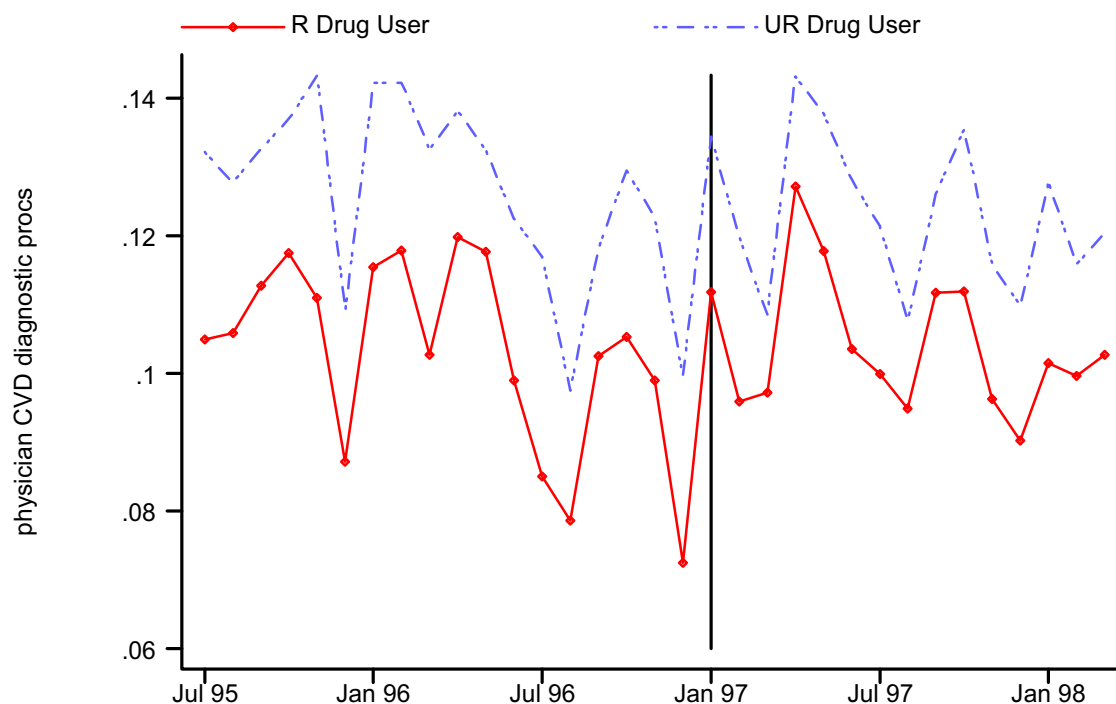


Figure 70 Probability of physician CVD diagnostic procedure, by CCBs RP exposure status, and month

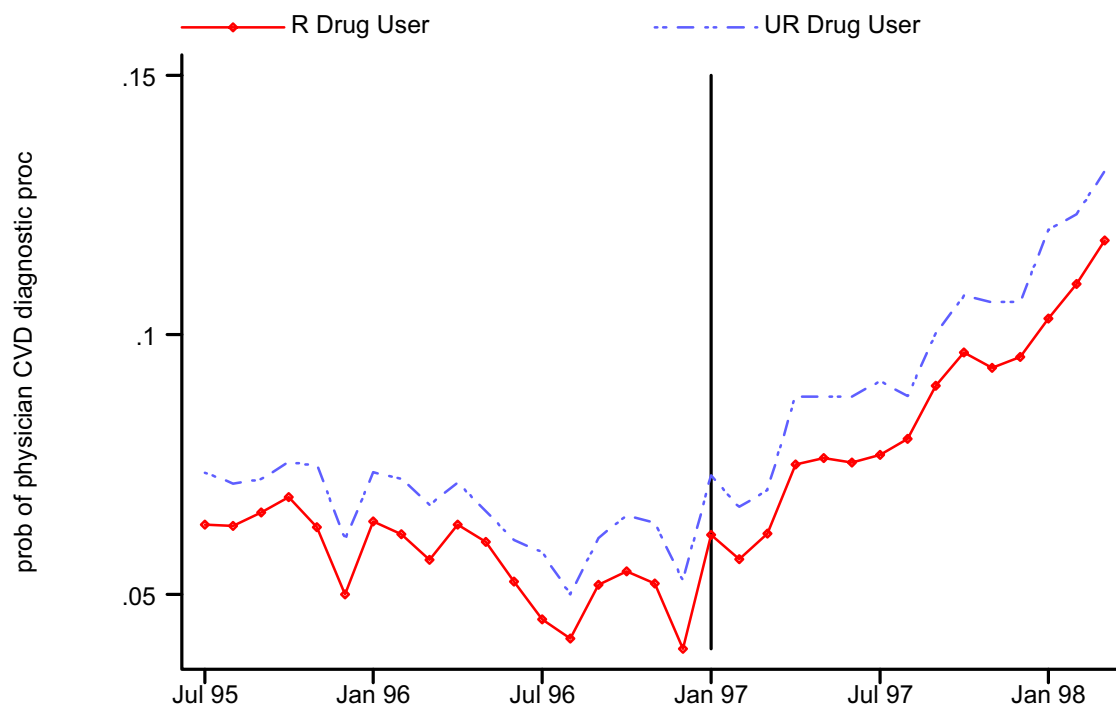


Figure 71 Mean number of physician CVD surgical procedures, by CCBs RP exposure status, and month

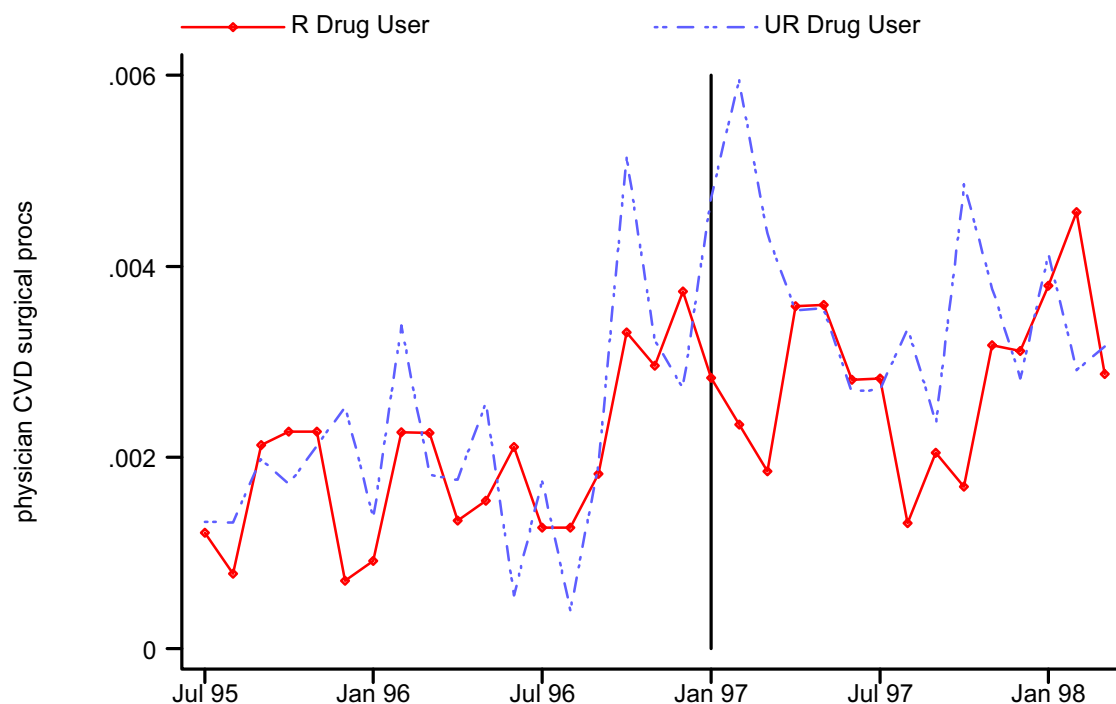


Figure 72 Probability of physician CVD surgical procedure, by CCBs RP exposure status, and month

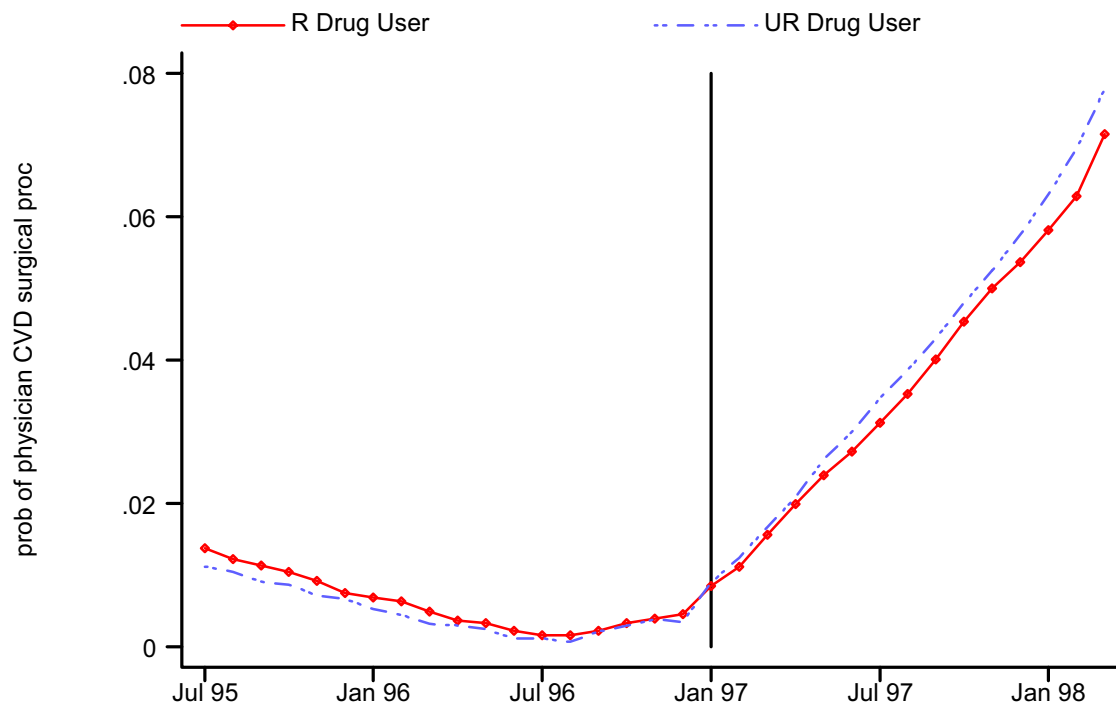


Figure 73 Mean number of hospital admission for cardiovascular or renal conditions, by CCBs RP exposure status, and month

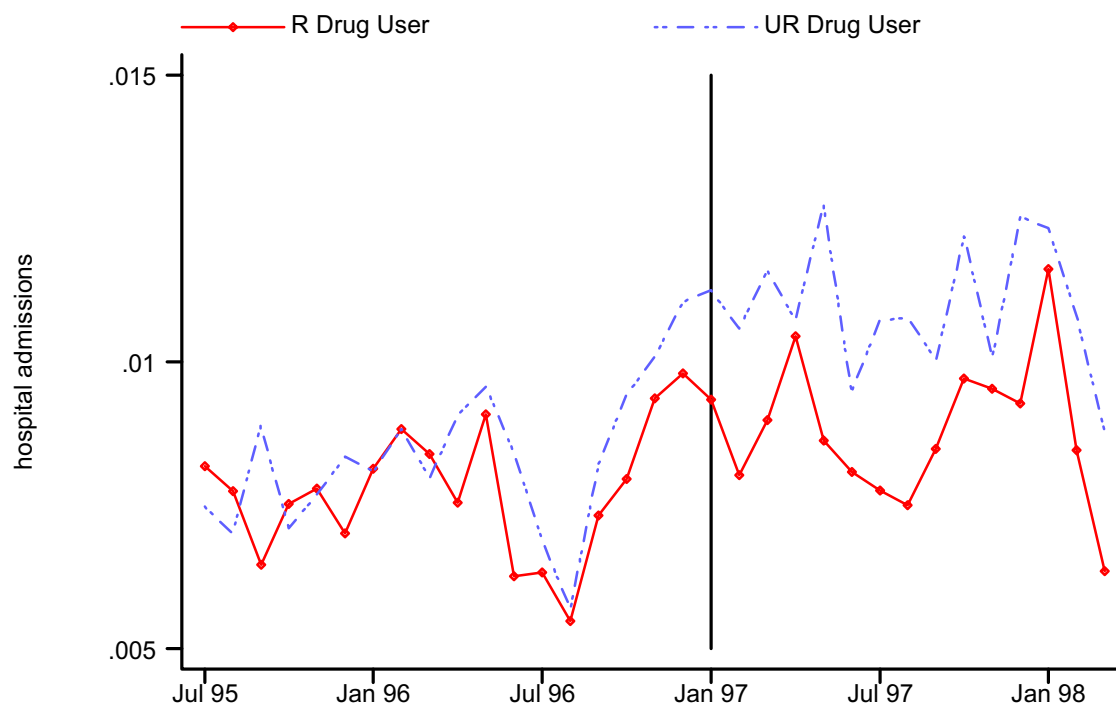


Figure 74 Probability of hospital admission for cardiovascular or renal condition, by CCBs RP exposure status, and month

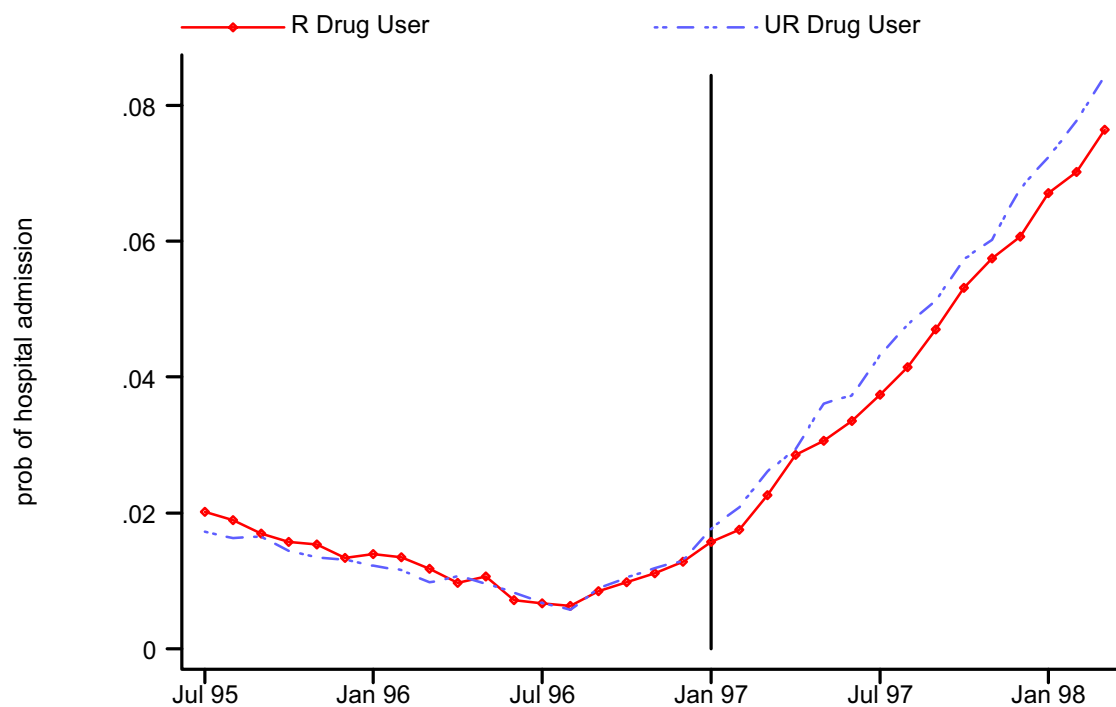


Figure 75 Mean number of days in hospital for cardiovascular or renal condition, by CCBs RP exposure status, and month

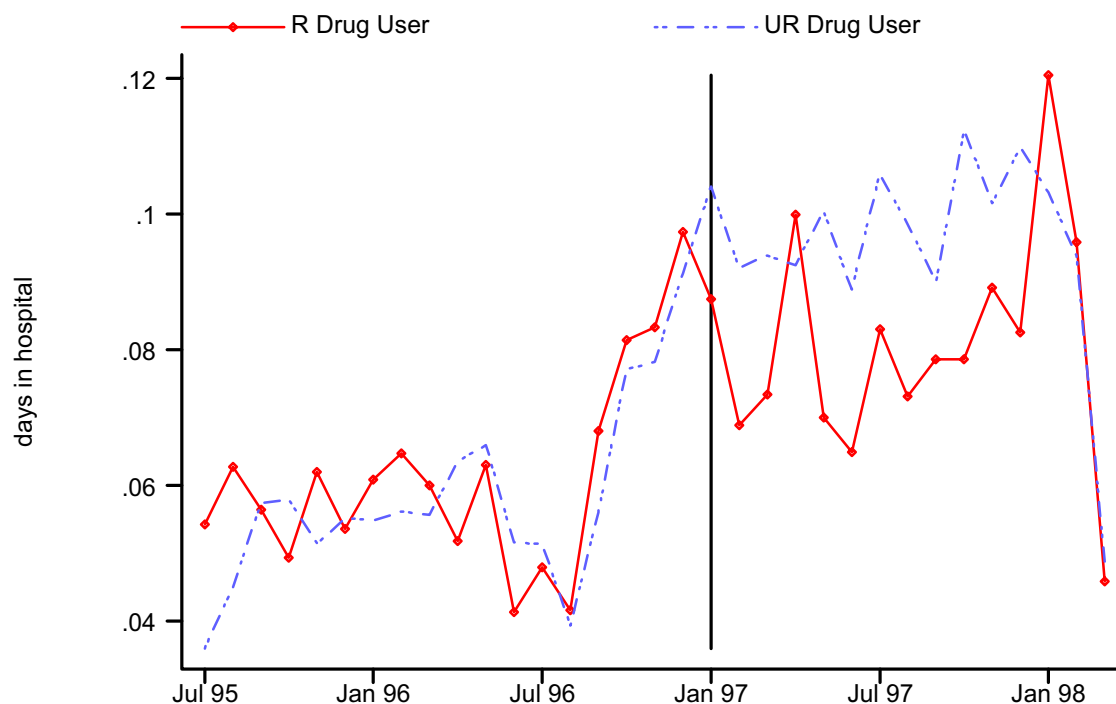


Figure 76 Probability of day in hospital for cardiovascular or renal condition, by CCBs RP exposure status, and month

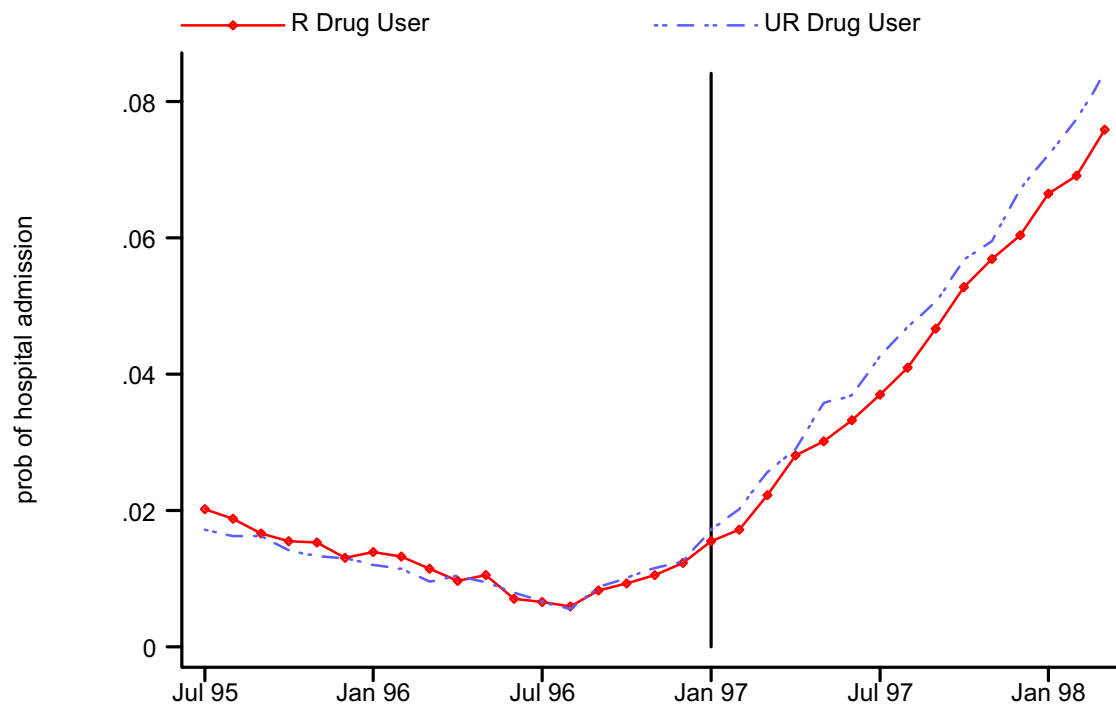


Figure 77 Mean number of revascularizations, by CCBs RP exposure status, and month

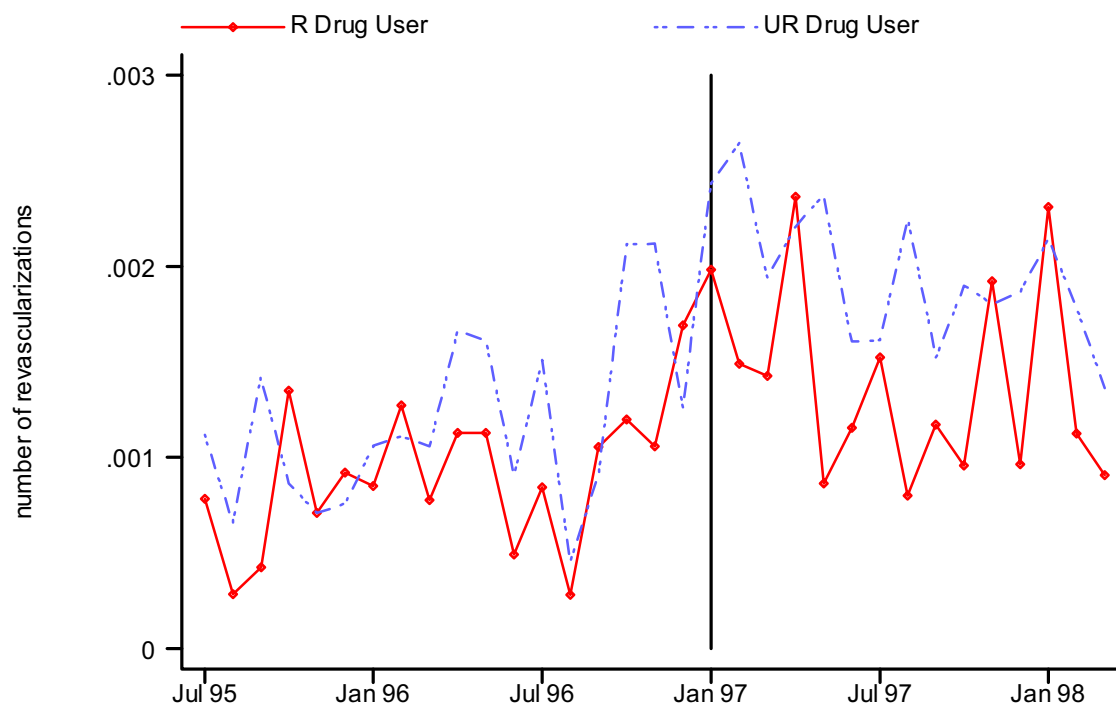


Figure 78 Probability of revascularization, by CCBs RP exposure status, and month

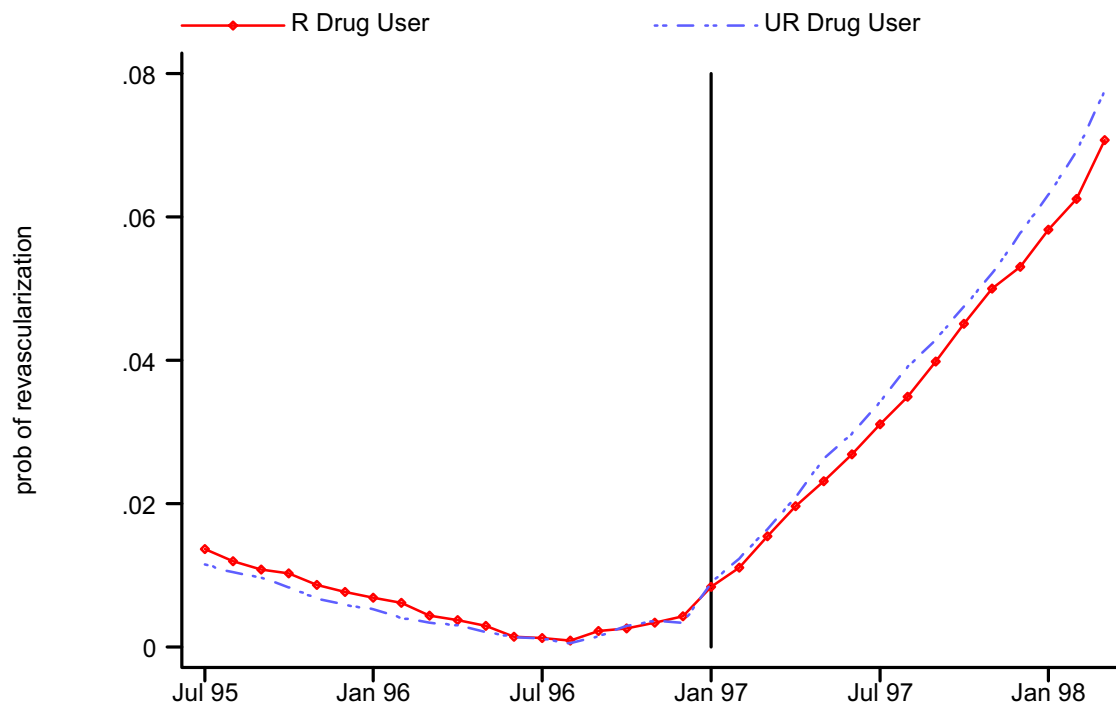


Figure 79 Mean number of prescriptions for sublingual nitroglycerin, by CCBs RP exposure status, and month

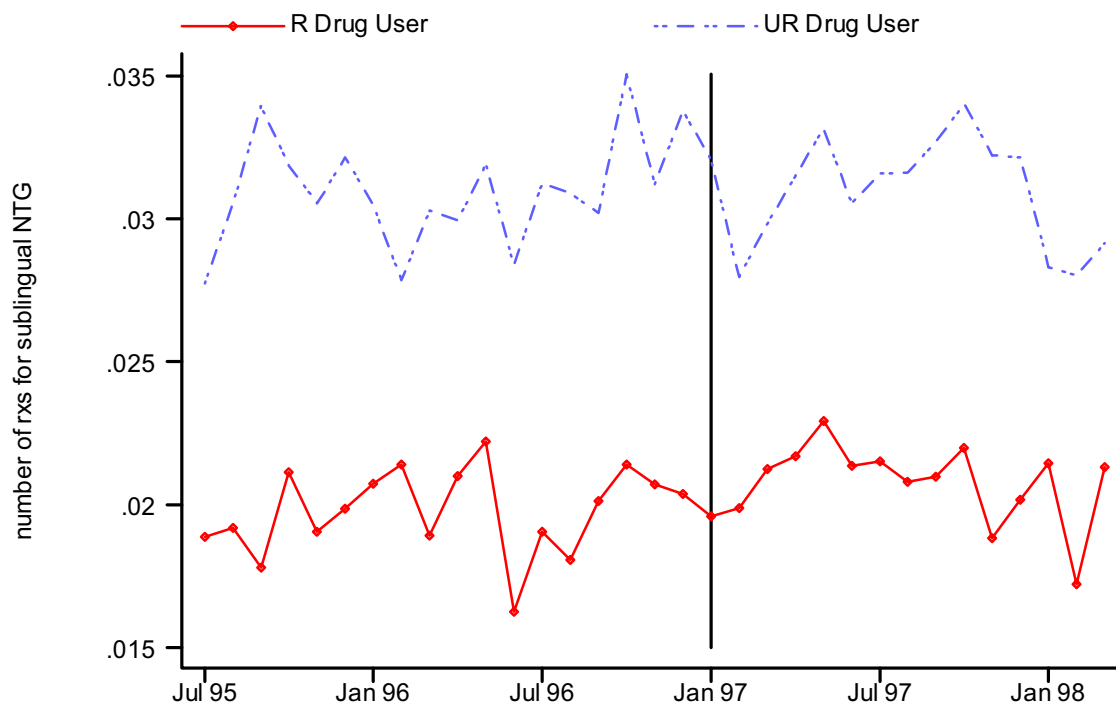
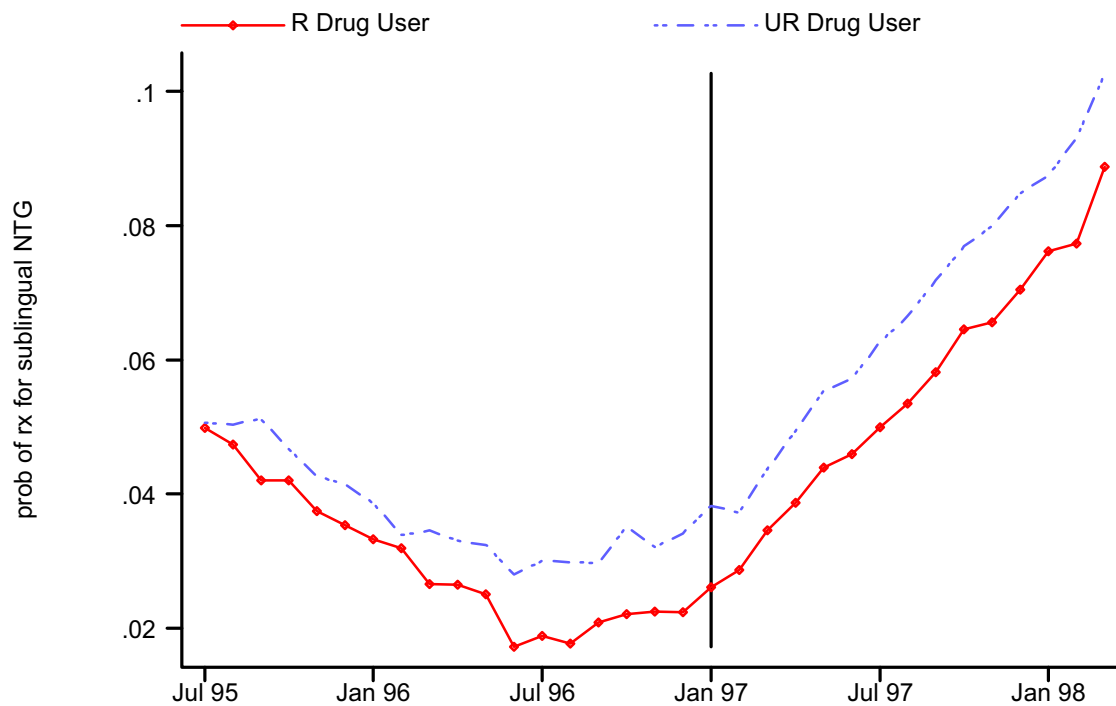


Figure 80 Probability of prescription for sublingual nitroglycerin, by CCBs RP exposure status, and month



4.2.7 Cost of ambulatory physician consultations

Table 35 presents fixed effect linear regression estimates of the effect of RP on the cost of ambulatory physician consultations, by drug group and time period. Our model estimated both short run costs (additional costs in the first 4 months of the introduction of the policy over and above any long run costs) and long run costs (additional costs starting with the introduction of the respective RP policies and ending with the last observation month, March 1998). Our model produced estimates of the additional cost per person exposed to RP per month. We found that those exposed to ACE inhibitors RP incurred an additional \$0.65 per month (95% CI: \$0.38 to \$0.93) in the longrun, and those exposed to CCBs RP incurred an additional \$0.40 per month (95% CI: \$0.17 to \$0.62) in the longrun. To get long run costs, we multiplied these estimates by the number of individuals who were exposed to the RP policy and multiplied again by the length of exposure post-RP.

The difference-in-differences design appeared to be appropriate for the cost models: The exposed and comparator groups in each of the 3 drug categories had similar trends in cost of physicians consultations before the introduction of the RP. This is confirmed by visual examination of the pre-RP trends displayed by drug category in the Figures below. Equally apparent from the figures is the effect of the delisting of several physician fee codes from the BC physician fee schedule in 1996 on costs to the BC Ministry of Health.

Table 35 Estimated effect of RP on costs of ambulatory physician consultations, with 95% confidence intervals, by drug group and time period (short run, long run, and annualized long run costs)

Drug Group	Time Frame	Additional cost of ambulatory physician consults	Lower 95% Confidence Interval	Upper 95% Confidence Interval
Nitrates	Short run (4 months after RP)	80,765	55,678	105,852
	Long run (introduction of RP to March 1998)	-598,168	-692,861	-503,475
	Total	-517,403		
	Long run (annualized value)	-281,806	-326,417	-237,194
ACE inhibitors	Short run (4 months after RP)	43,163	-3,945	90,271
	Long run (introduction of RP to March 1998)	265,280	152,686	377,874
	Total	308,443		
	Long run (annualized value)	221,159	127,291	315,027
CCBs	Short run (4 months after RP)	27,570	8,419	46,720
	Long run (introduction of RP to March 1998)	82,052	35,922	128,183
	Total	109,622		
	Long run (annualized value)	67,603	29,596	105,610

The additional costs of physician consults varied by drug category: in the short run, the additional costs associated with the implementation of nitrates RP was relatively high. This is remarkable given that relatively few seniors (10,958) were exposed to nitrates, compared to

28,234 for ACE inhibitors and 14,234 for CCBs. In the long run, the costs varied even more: costs were in fact negative for nitrates, \$265,000 for ACE inhibitors and \$110,000 for CCBs.

Figure 81 Monthly average cost of ambulatory physician consultations per senior, by month and nitrates RP exposure status (introduction of RP indicated)

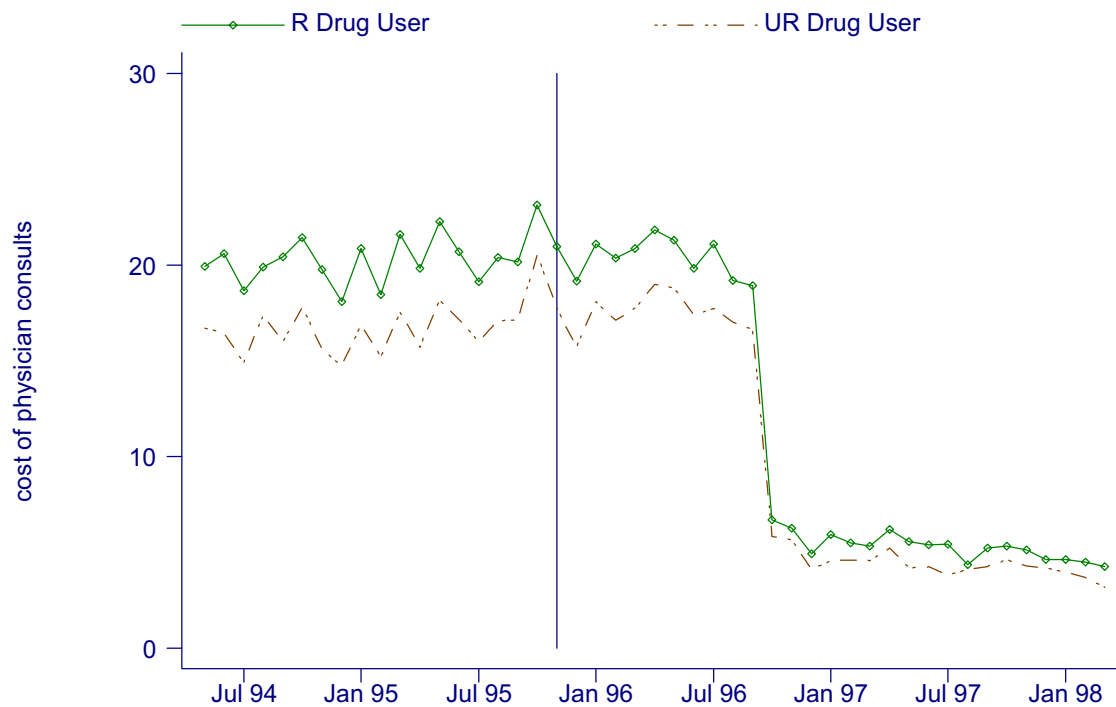


Figure 82 Monthly average cost of ambulatory physician consultations per senior, subject and month-specific fixed effects removed, by month and nitrates RP exposure status. Lowess smoothed data (bandwidth = 50%)

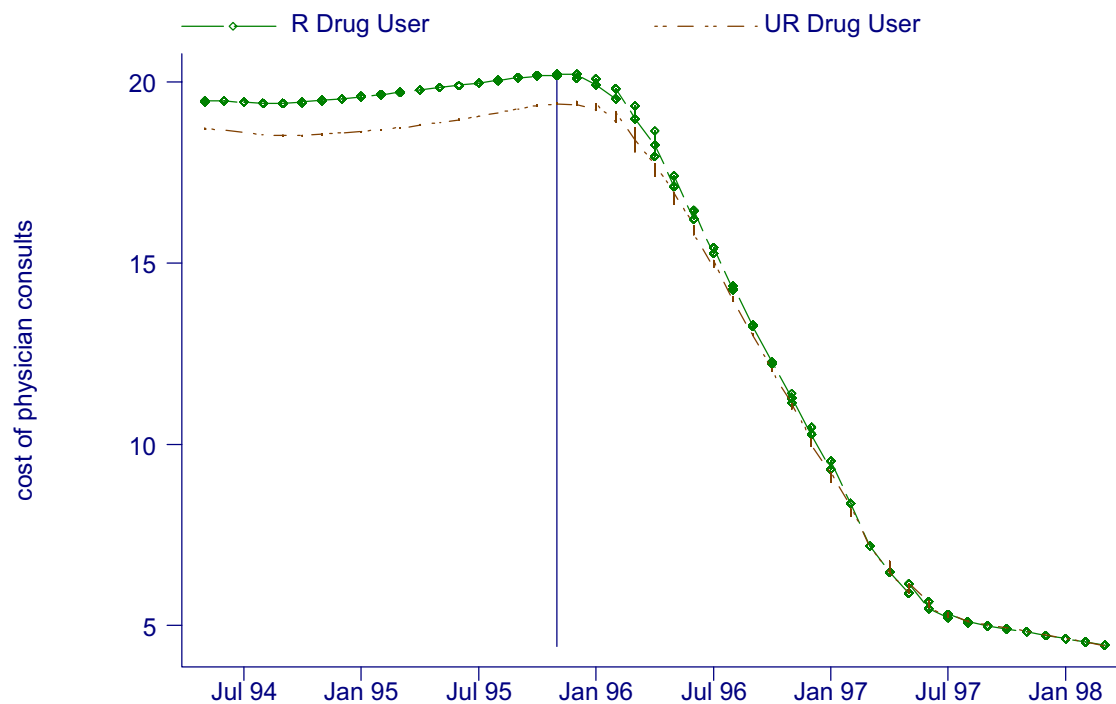


Figure 83 Monthly average cost of ambulatory physician consultations per senior, by month and ACE inhibitor RP exposure status (introduction of RP indicated)

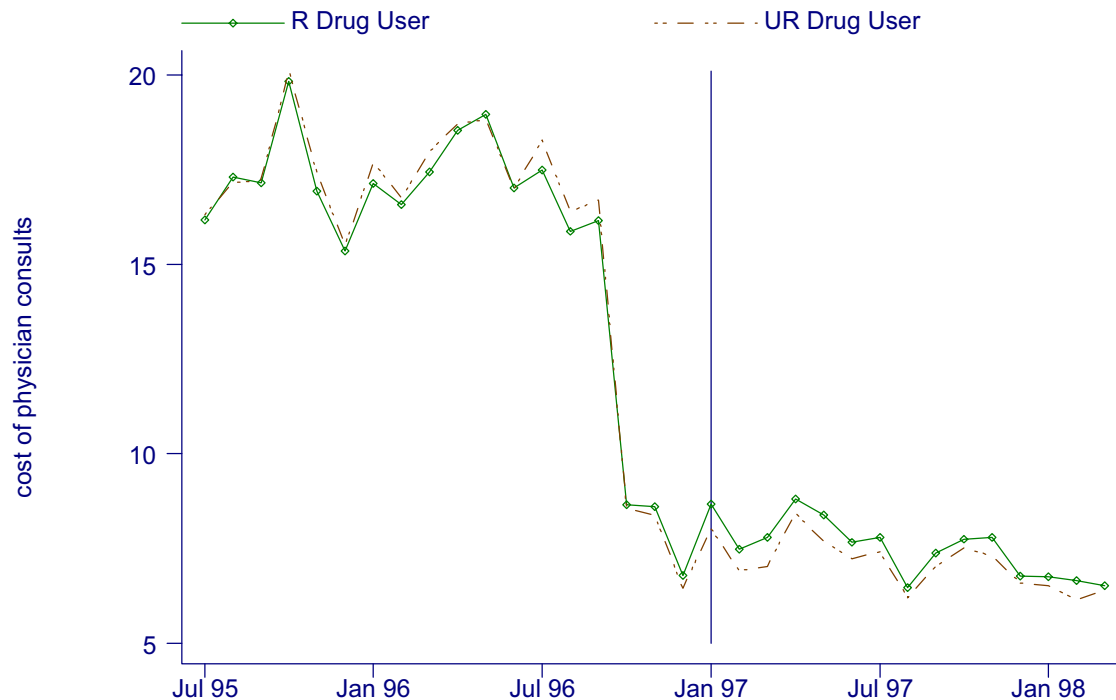


Figure 84 Monthly average cost of ambulatory physician consultations per senior, subject and month-specific fixed effects removed, by month and ACE inhibitor RP exposure status. Lowess smoothed data (bandwidth = 50%)

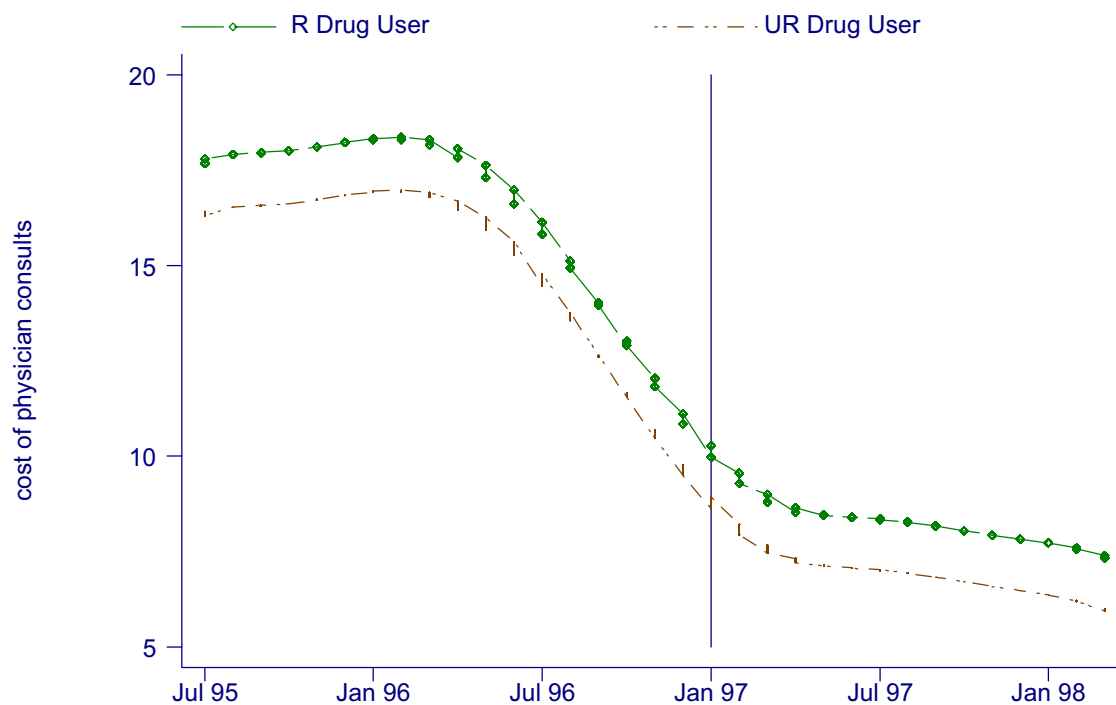


Figure 85 Monthly average cost of ambulatory physician consultations per senior, by month and CCB RP exposure status (introduction of RP indicated)

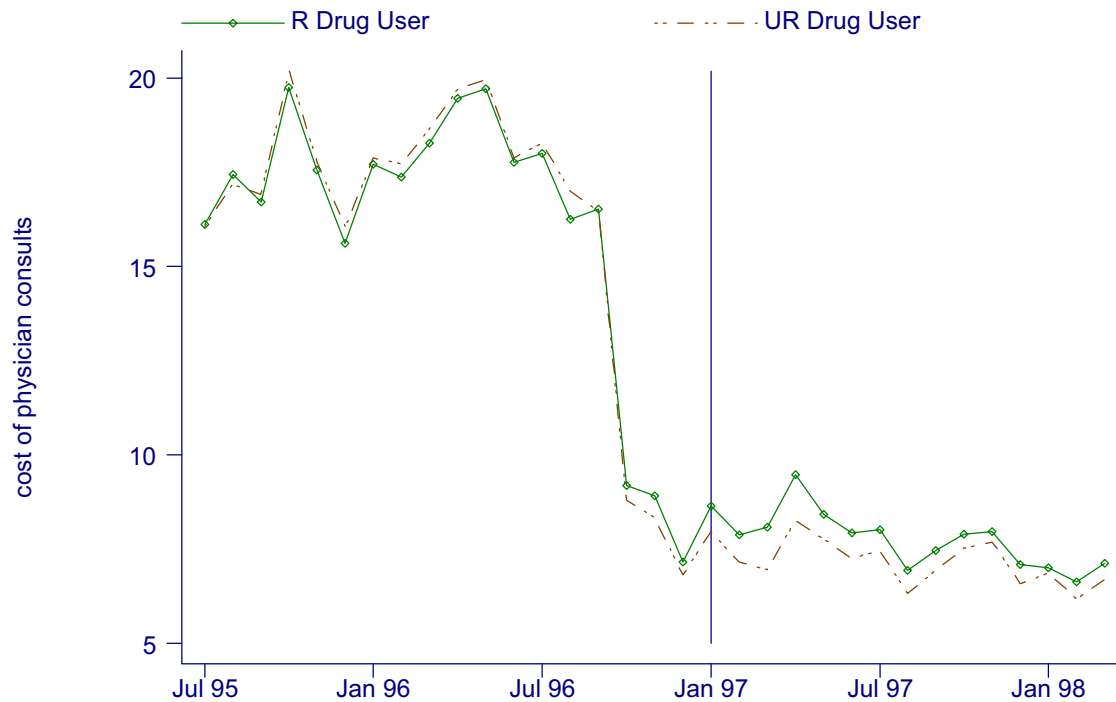
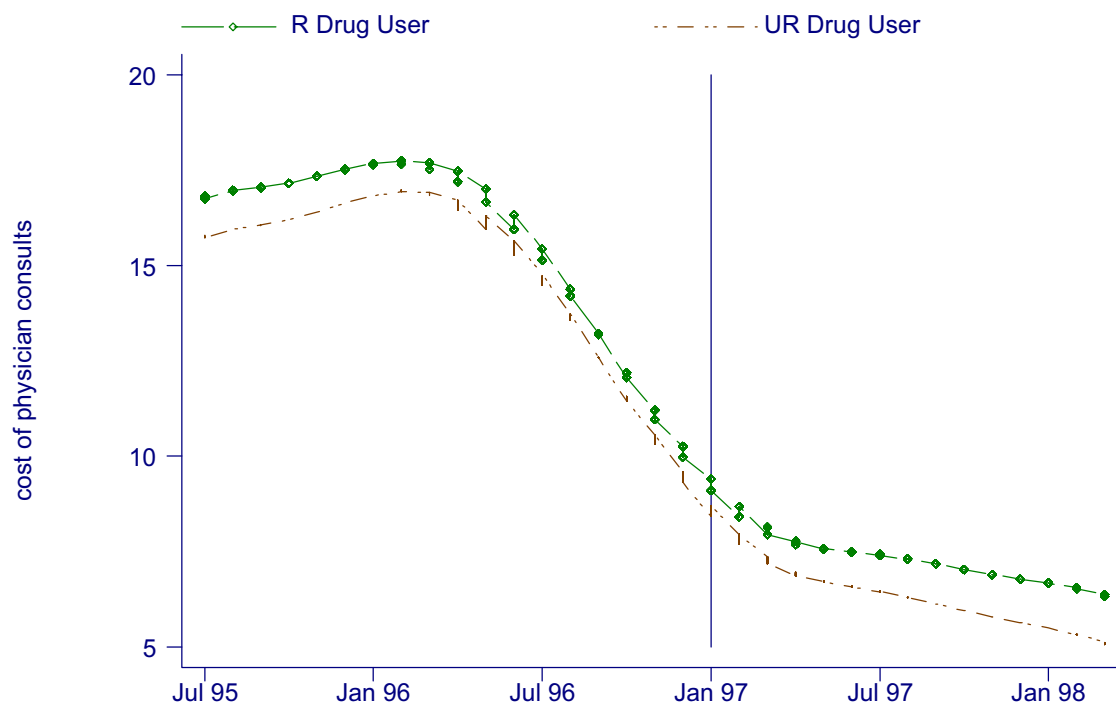


Figure 86 Monthly average cost of ambulatory physician consultations per senior, subject and month-specific fixed effects removed, by month and CCB RP exposure status. Lowest smoothed data (bandwidth = 50%)



4.2.8 Probability of exemption and amount paid out of pocket

Table 36 presents estimates of the effect of low income status on: the probability of exemption from RP and, in the sample of those not exempted from RP, the probability that the patient paid more than \$1 for Restricted drugs during the year following the introduction of RP, as well as the amount paid in the subsample of payers. The difference in payment for those with low income, relative to those with higher income, is presented in both absolute dollar terms and as a relative difference (using the model of log amount paid), the amount paid by the low income as a fraction of the amount paid by the higher income subjects. If there is measurement error in the low income indicator then the absolute value of the estimates represents the lower bound on the effect of income on the outcomes studied.

Table 36 Estimated effects of low income status on probability of exemption and amount paid out of pocket

Drug Group	Outcome variable							
	Probability of exemption from RP		Probability of Payment > \$1		Amount paid in subsample of payers		Log Amount paid in subsample of payers	
	Estimate	p-value	Estimate	p-value	Estimate	p-value	Estimate	p-value
Nitrates	2.0%	0.032	-5.0%	<0.001	-\$10.88	0.015	-12.0%	0.010
ACE inhibitors	0.5%	0.427	-4.0%	<0.001	-\$10.33	0.043	-6.0%	0.019
CCBs	-0.2%	0.803	-4.0%	0.018	-\$6.48	0.012	-14.0%	0.001

We find that among those using ACE inhibitors or CCBs, those with low income have the same probability of exemption as do those with high income. Among nitrates users, those with low income are at least 2% more likely to be exempted than those with high income. Among the subsample of those not exempted from RP, low income status has some effect of the probability and amount paid. Those with low income are between at least 4-5% less likely to pay more than \$1 for Restricted drugs over the year following the introduction of RP. Of those that do pay more than \$1, low income seniors pay between at least \$6.48 to \$10.88 less than do higher income seniors. These represent proportional reductions of between at least 6%-14%, depending on the drug class.

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Appendix 1 Description of British Columbia Medical Services Plan Fee Schedule Items, by category of service

Physician consultations

Fee Item Description

13110CONSULTATION - (IN/OUT OF OFFICE) AGE 70+
110CONSULTATION (IN OR OUT OF OFFICE): AGE 0-69
7810CONSULTATION, CARDIO-THORACIC
7812CONSULTATION, LIMITED OR REPEAT, CARDIO-THORACIC
3970INITIAL EXAM.-WILL INCLUDE CLINICAL EXAM.AND EXP
107VISIT (IN OR OUT OF OFFICE) - SUBSEQUENT
100VISIT IN OFFICE (AGE 0 - 69)
7809VISIT, HOME, CARDIO-THORACIC
7807VISIT, OFFICE, CARDIO-THORACIC

Emergency and Hospital visits

Fee Item Description

118CAESAREAN SECTION-ATTENDANCE
136CHIRO EMERG VISIT, NIGHT SUNDAY OR STAT.
94006CLINICAL PATHOLOGY, DIRECTIVE CARE
94005CLINICAL PATHOLOGY, EMERGENCY VISIT
94008CLINICAL PATHOLOGY, HOSPITAL VISIT
9706DIRECTIVE CARE
1706DIRECTIVE CARE - PHYSICAL MEDICINE
7006DIRECTIVE CARE - GENERAL SURGERY
204DIRECTIVE CARE BY CONSULTANTS
306DIRECTIVE CARE, INTERNAL MEDICINE
406DIRECTIVE CARE, NEUROLOGY
506DIRECTIVE CARE, PAEDIATRICS
1018EMERGENCY AT NIGHT, ANAESTHESIA
102EMERGENCY VISIT
5005EMERGENCY VISIT
9705EMERGENCY VISIT
106EMERGENCY VISIT
7005EMERGENCY VISIT - GENERAL SURGERY
2005EMERGENCY VISIT - OPHTHALMOLOGY
2505EMERGENCY VISIT - OTOLARYNGOLOGY
109FIRST HOSPITAL VISIT
122GROUP COUNSELLING-2ND HOUR/PER HALF OR MAJOR PART
8884HOSPITAL IN-PATIENT PER DIEM AUTHORIZED USUAL AND
8887HOSPITAL IN-PATIENT PER DIEM RATE - AUTHORIZED B.C
8888HOSPITAL IN-PATIENT PER DIEM RATE - VACATION (O.O.P.)
8883HOSPITAL IN-PATIENT PER DIEM RATE FOR NEWBORN CARE
2008HOSPITAL VISIT - OPHTHALMOLOGY

Fee Item Description

1108 HOSPITAL VISIT - ANAESTHESIA
51008 HOSPITAL VISIT - ORTHOPAEDICS
127 HOSPITAL VISIT FOR TERMINAL CARE
9910 INITIAL VISIT - NURSING HOME - PHYSICAL THERAPY
164 INSTITUTIONAL VISIT - SESSIONAL RATE 1/2 HR
158 INSTITUTIONAL VISIT - SESSIONAL RATE INITIAL 3
1811 LEVEL I EMERGENCY CARE - DAY
1821 LEVEL I EMERGENCY CARE - EVENING
1831 LEVEL I EMERGENCY CARE - NIGHT
1841 LEVEL I EMERGENCY CARE - SAT, SUN, OR STAT HOL
1812 LEVEL II EMERGENCY CARE - DAY
1822 LEVEL II EMERGENCY CARE - EVENING
1832 LEVEL II EMERGENCY CARE - NIGHT
1842 LEVEL II EMERGENCY CARE - SAT, SUN OR STAT HOL
1813 LEVEL III EMERGENCY CARE - DAY
1823 LEVEL III EMERGENCY CARE - EVENING
1833 LEVEL III EMERGENCY CARE - NIGHT
1843 LEVEL III EMERGENCY CARE - SAT, SUN OR STAT HOL
3509 MEDICAL MANAGEMENT OF INFLAMMATORY ORAL DISEASE
9708 MEDICAL MICROBIOLOGY - SUBSEQUENT HOSPITAL VISIT
146 NATUROPATHIC PHYSICIANS - EMERGENCY VISIT
119 NEWBORN CARE, ROUTINE, IN HOSPITAL
113 ON CALL, ON SITE HOSPITAL VISIT - EVENING
105 ON CALL, ON SITE HOSPITAL VISIT - NIGHT
123 ON CALL, ON SITE HOSPITAL VISIT - SAT, SUN OR HOLS
5008 ORTHOPAEDICS - SUBSEQUENT HOSPITAL VISIT
166 PODIATRISTS SERVICE - EMERGENCY VISIT AFTER 8:00
159 PODIATRISTS SERVICE - INSTITUTIONAL VISITS
9912 PROLONGED VISIT AT NURSING HOME, THERAPY RENDERED
124 RE-ISSUE
125 RE-ISSUE
31006 RHEUMATOLOGY - DIRECTIVE CARE
31005 RHEUMATOLOGY - EMERGENCY VISIT, SPECIALLY CALLED
31008 RHEUMATOLOGY - SUBSEQUENT HOSPITAL VISIT
3785 SALIVARY GLAND PROCEDURES: HOSPITAL VISIT, FOLLOW-
7008 SUBSEQUENT HOSPITAL VISIT - GENERAL SURGERY
2508 SUBSEQUENT HOSPITAL VISIT - OTOLARYNGOLOGY
9911 SUBSEQUENT VISIT AT NURSING HOME-THERAPY RENDERED
128 SUPPORTIVE CARE
114 VISIT NURSING HOME ONE OR MULTIPLE PATIENTS
115 VISIT NURSING HOME ONE PATIENT SPECIAL DAY CALL
112 VISIT, EMERGENCY
111 VISIT, EMERGENCY HOME
7805 VISIT, EMERGENCY, CARDIO-THORACIC
205 VISIT, EMERGENCY, DERMATOLOGY
305 VISIT, EMERGENCY, INT. MED
405 VISIT, EMERGENCY, NEUROLOGY

Fee Item Description

3005 VISIT, EMERGENCY, NEUROSURGERY
4005 VISIT, EMERGENCY, OB&G
505 VISIT, EMERGENCY, PAEDIATRICS
1705 VISIT, EMERGENCY, PHYSICAL MEDICINE
6005 VISIT, EMERGENCY, PLASTIC SURGERY
605 VISIT, EMERGENCY, PSYCHIATRY
8005 VISIT, EMERGENCY, UROLOGY
108 VISIT, HOSPITAL
7808 VISIT, HOSPITAL, CARDIO-THORACIC
208 VISIT, HOSPITAL, DERMATOLOGY
308 VISIT, HOSPITAL, INT. MED
408 VISIT, HOSPITAL, NEUROLOGY
3008 VISIT, HOSPITAL, NEUROSURGERY
4008 VISIT, HOSPITAL, OB&G
508 VISIT, HOSPITAL, PAEDIATRICS
1708 VISIT, HOSPITAL, PHYSICAL MEDICINE
6008 VISIT, HOSPITAL, PLASTIC SURGERY
608 VISIT, HOSPITAL, PSYCHIATRY
8008 VISIT, HOSPITAL, UROLOGY
19155 WCB - INSTITUTIONAL VISIT - MASSAGE THERAPY
129 WCB EMERGENCY CALL OUT

CVD Surgical Procedures

Fee Item Description

7915 1ST ASSIST AT OPEN HEART SURGERY: <= \$1027.00
7917 1ST ASSIST AT OPEN HEART SURGERY: > \$1027.00
7916 2ND & 3RD ASSISTS AT OPEN HEART SURG: <= \$1027.00
7918 2ND & 3RD ASSISTS AT OPEN HEART SURG: > \$1027.00
7252 ABDOMINAL ANEURYSM, WITH GRAFTING
7822 ANEURYSM RUPTURED THORACIC
7822 ANEURYSM RUPTURED THORACIC
7821 ANEURYSM THORACIC
7821 ANEURYSM THORACIC
982 ANGIOPLASTY, PERCUTANEOUS TRANSLUMINAL
7235 AORTA AND/OR ILIAC BYPASS GRAFT - BILATERAL
7232 AORTA AND/OR ILIAC BYPASS GRAFT - UNILATERAL
7827 AORTIC DISSECTION REPAIR (THORACIC)
7827 AORTIC DISSECTION REPAIR (THORACIC)
7240 AORTO-FEMORAL AND ILIO-FEMORAL BYPASS, UNILATERAL
7243 AORTO-ILIAC, AORTO-FEMORAL, ILIO-FEMORAL BYPASS
7920 ASSIST AT OPEN HEART SURG: > 4 HRS, PER 15 MINS
7236 A-V FISTULA WITH BYPASS GRAFT IN LIMB SALVAGE
7278 AXILLO-FEMORAL BYPASS GRAFT (AUTOGENOUS VEIN)
7226 AXILLO-FEMORAL BYPASS GRAFT (SYNTHETIC)/UNILATERAL
7227 AXILLO-FEMORAL BYPASS GRAFT(SYNTHETIC)/BILATERAL

Fee Item Description

7264 BYPASS GRAFT (AUTOGENOUS VEIN) - ILIAC
7266 BYPASS GRAFT (AUTOGENOUS VEIN) - POPLITEAL
7263 BYPASS GRAFT (AUTOGENOUS VEIN) - AORTA
7265 BYPASS GRAFT (AUTOGENOUS VEIN) - FEMORAL
7846 CARDIAC MASSAGE FOR CARDIAC ARREST
7846 CARDIAC MASSAGE FOR CARDIAC ARREST
7919 CARDIAC SURGERY OTHER SPECIALIST
7237 CAROTID ARTERIES - BYPASS GRAFT (SYNTHETIC)
7909 CORONARY ARTERY BYPASS GRAFT - EACH ADDIT. ARTERY
7909 CORONARY ARTERY BYPASS GRAFT - EACH ADDIT. ARTERY
7908 CORONARY ARTERY BYPASS GRAFT - ONE ARTERY
7908 CORONARY ARTERY BYPASS GRAFT - ONE ARTERY
7231 EMBOLECTOMY - ONE SIDE
7230 EMBOLECTOMY - TRUNK OR EXTREMITIES
7238 FEMORAL BYPASS GRAFT (SYNTHETIC)
7277 FEMORO-FEMORAL CROSSOVER BYPASS GRAFT/AUTOGENOUS
13 INJECTION, INTRA-ARTERIAL
7233 INOMINATE - NECK OR THORACIC - BYPASS GRAFT
7242 INTRAGUINAL - ANTERIOR, POST TIBIAL OR PERONEAL
7340 NON-IPSI LATERAL LONG SAPHE NOUS GRAFT - AUTOGENOUS
13199 OPEN HEART SURGERY ADDITIONAL SPECIALIST
8630 PERCUTANEOUS TRANSLUMINAL ANGIOPLASTY
7824 RESECTING ANEURYSM OF THE VENTRICLE
7824 RESECTING ANEURYSM OF THE VENTRICLE
7825 RESECTING ANEURYSM WITH OTHER PROCEDURE
7825 RESECTING ANEURYSM WITH OTHER PROCEDURE
7281 RESECTION OF ABDOMINAL ANEURYSM
7826 RESECTION OF AORTIC ARCH ANEURYSM
7826 RESECTION OF AORTIC ARCH ANEURYSM
7254 RUPTURED ANEURYSM, WITH GRAFTING
7341 SHORT SAPHE NOUS GRAFT
7234 SUBCLAVIAN - NECK OR THORACIC - BYPASS GRAFT
7342 SUPERFICIAL FEMORAL VEIN GRAFT(EXTRA)
7267 SYNCHRONOUS COMBINED BYPASS GRAFT - EXTREMITIES
7229 THROMBECTOMY WITH OR WITHOUT ANGIOPLASTY

CVD Diagnostic Procedures

Fee Item Description

812 ANGIOCARDIOGRAM SELECTIVE
8624 ANGIOGRAM, THORACIC OR ABDOMINAL , SINGLE FILM
8626 ANGIOGRAM, THORACIC OR ABDOMINAL, MULT NON-SELECT
8627 ANGIOGRAM, THORACIC OR ABDOMINAL, MULT SELECTIVE
8625 ANGIOGRAM, THORACIC OR ABDOMINAL, SELECTIVE
8616 ANGIOGRAPHY CEREBRAL X-RAY - BILATERAL
8615 ANGIOGRAPHY CEREBRAL X-RAY - UNILATERAL

Fee Item Description

8618 ANGIOGRAPHY PERIPHERAL - BILATERAL
8617 ANGIOGRAPHY PERIPHERAL - UNILATERAL
890 AORTOGRAM ABDOMINAL
8620 AORTOGRAPHY (AORTOGRAPHY PLUS PERIPHERAL ANGIOGRAP
892 ARTERIOGRAM - CAROTID PERCUTANEOUS, UNILATERAL
891 ARTERIOGRAM - CAROTID PERCUTANEOUS; BILATERAL
894 ARTERIOGRAM - CEREBRAL
893 ARTERIOGRAM - FEMORAL OR AXILLARY
722 ARTERIOGRAPHY, OPERATIVE
9862 CARDIAC FUNCTION STUDIES, DYNAMIC
95010 CARDIAC STRESS EJECTION FRACTION
322 CARDIOANGIOGRAM INTERNIST PART
846 CARDIOLOGY ASSIST- AFTER ONE HOUR, FOR EACH 15 MIN
845 CARDIOLOGY ASSIST FOR FIRST HOUR OR FRACTION
8676 CAROTID IMAGING - DUPLEX SCANNING OF NECK VESSELS
8672 CAROTID IMAGING - EXTRA CRANIAL VESSEL HEAD/NECK
810 CATHETERIZATION RIGHT HEART
9897 CORONARY ADMIN OF RADIO PARTICLES - TRANSCATHETER
9898 CORONARY PERFUSION WITH RADIO PARTICLES
8671 DIAGNOSTIC ULTRASOUND, DOPPLER STUDIES, PERIPHERAL
841 DIRECT ANGIOGRAPHY CORONARY
839 DIRECT INTRA-CORONARY STREPTOKINASE THROMBOLYSIS
8679 DOPPLER ECHOCARDIOGRAPHY
317 ECG AND INTERPRETATION HOME (INT. MED)
316 ECG AND INTERPRETATION OFFICE (INT. MED.)
93120 ECG TRACING
318 ECG, INTERPRETATION ONLY, INT. MED.
391 ECHOCARDIOGRAM - 2-D/ M-MODE
8643 ECHOCARDIOGRAM - M-MODE
8638 ECHOCARDIOGRAM - REAL TIME
8661 ECHOCARDIOGRAM-COMBINED
321 ELECTROCARDIOGRAM MASTERS 2-STEP- TECHNICAL FEE
9401 ELECTROCARDIOGRAM TRACING
813 ERGONOVINE TESTING, CORONARY ARTERY SPASM
8662 EXERCISE ECHOCARDIOGRAPHY
334 GRADED EXERCISE TEST
1731 GRADED EXERCISE TEST - PROFESSIONAL
335 GRADED EXERCISE TEST - PROFESSIONAL FEE
1730 GRADED EXERCISE TEST - TECHNICAL
336 GRADED EXERCISE TEST - TECHNICAL FEE
1732 GRADED EXERCISE TEST - TOTAL
801 INTRA-ARTERIAL CANNULATION
366 INTRACARDIAC ELECTROPHYSIOLOGICAL MAPPING
367 INTRACARDIAC ELECTROPHYSIOLOGICAL MAPPING-RESTUDY
835 LEFT VENTRIC. AND FEM. ARTERY PUNCTURES-SPECIALIST
836 LEFT VENTRIC. AND FEM. ARTERY PUNCTURES-SURGEON
9424 MASTERS 2-STEP ELECTROCARDIOGRAM, TECH. FEE

Fee Item Description

95035 MYOCARDIAL PERFUSION
842 PERCUT. TRANSLUM. COR. ANGIOPL. - ADDITIONAL SITE
840 PERCUTANEOUS TRANSLUMINAL CORONARY ANGIOPLASTY
9866 PERFUSION STUDY, ADDITION TO MAJOR SCAN
9865 PERFUSION STUDY, DONE ALONE
848 RADIOACTIVE MYOCARDIAL PERFUSION STUDY
9863 RADIONUCLIDE CARDIAC VENTRICULOGRAPHY
95040 RADIONUCLIDE CARDIAC VENTRICULOGRAPHY WITH STRESS
827 RETROGRADE LEFT HEART CATHETERIZATION - EXTRA
346 SCANNING OF 24 HOUR ELECTROCARDIOGRAM
349 SCANNING OF 24 HR. E.C.G. - LEVEL 1
348 SCANNING OF 24 HR. E.C.G.- TECHNICAL FEE
347 SCANNING OF 24 HR. E.C.G.-PROFESSIONAL FEE
363 SCANNING OF 24-HR. E.C.G. - LEVEL 2
364 SCANNING OF 24-HR. E.C.G. - LEVEL 3
365 SCANNING OF 24-HR. E.C.G. - LEVEL 4
340 SCANNING OF 8 HOUR ELECTROCARDIOGRAM
341 SCANNING OF 8 HR. E.C.G. - PROFESSIONAL FEE
342 SCANNING OF 8 HR. E.C.G. - TECHNICAL FEE
843 SELECTIVE ARTERIOGRAPHY OF ABDOMINAL BRANCH
847 SELECTIVE ARTERIOGRAPHY OF THORACIC AORTIC BRANCH
7020 SURGEONS PART-CARDIOANGIOGRAM
9854 THALLIUM MYOCARDIAL SCAN
357 TRANS-ESOPHAGEAL ECHOCARDIOGRAPHY
830 TRANS-SEPTAL LEFT HEART CATHETERIZATION
8666 TREADMILL STRESS WITHOUT MONITORING PHYSICIAN
8665 TREADMILL STRESS; WITH MONITORING PHYSICIAN
895 VENTRICULOGRAM

Renal Surgical & Diagnostic Procedures

Fee Item Description

8660 ABDOMINAL DUPLEX- NATIVE/ TRANSPLANT LIVER/KIDNEY
725 AIR INSUFFLATION - PERIRENAL
390 CARE OF RENAL TRANSPLANT PATIENT
8101 EXPLORATION RENAL AND PERIRENAL TISSUES
7761 IMPLANTATION OF KIDNEY GRAFT - VASCULAR SURGEON
7760 IMPLANTATION OF KIDNEY GRAFT -UROLOGIST
8106 NEPHRECTOMY - ECTOPIC KIDNEY
8115 NEPHROPEXY
8114 PYELOPLASTY INCLUDES NEPHROPEXY & MGMT OF ABERRANT
8649 RENAL B SCAN
742 RENAL BIOPSY
8112 RENAL BIOPSY-OPEN (AS AN INDEPENDENT PROCEDURE)
95050 RENAL BLEEDING SCAN
7262 RENAL BYPASS GRAFT (AUTOGENOUS VEIN)

Fee Item Description

7245 RENAL BYPASS GRAFT (SYNTHETIC)
8210 RENAL FUNCTION STUDIES-DIFFERENTIAL
95060 RENAL IMAGING/ WITHOUT PHARMACEUTICALS
95055 RENAL IMAGING/PHARMACEUTICALS
9847 RENAL SCAN, STATIC
7289 SUPRA-RENAL AORTIC CROSSCLAMP
8113 SYMPHYSIOTOMY AND NEPHROPEXY OR NEPHRECTOMY IN HOR
7762 TRANSPLANTATION FROM CADAVER WITH NECESSARY KIDNEY

Renal Dialysis

Fee Item Description

324 CHRONIC RENAL FAILURE - INSERTION - AV BYPASS
355 DIALYSIS ACUTE RENAL FAILURE, PERITONEAL
350 DIALYSIS ACUTE RENAL, HEMODIALYSIS
358 DIALYSIS CHRONIC RENAL (HEMODIALYSIS)

Appendix 2 Summary statistics of the characteristics of those taking nitrates, ACE inhibitors and CCBs, by RP exposure status.

Descriptive statistics, Nitrate users, by RP exposure status.

Covariate Description	Unrestricted Drug User (n=1,760)					Restricted Drug User (n = 11,155)				
	Mean	Median	Std. Dev.	Min.	Max.	Mean	Median	Std. Dev.	Min.	Max.
age at RP of Nitrates: Nov 1, 1995	79.06	78.92	6.46	65.55	99.67	79.04	78.97	6.44	65.52	106.67
=1 if male	0.45	0.00	0.50	0.00	1.00	0.42	0.00	0.49	0.00	1.00
=1 if female	0.53	1.00	0.50	0.00	1.00	0.56	1.00	0.50	0.00	1.00
=1 if unknown sex	0.02	0.00	0.14	0.00	1.00	0.02	0.00	0.15	0.00	1.00
interaction between age and female	42.10	69.76	40.10	0.00	97.25	44.46	71.11	39.79	0.00	106.67
=1 if received MSP premium subsidy 12 months prior to RP	0.55	1.00	0.50	0.00	1.00	0.56	1.00	0.50	0.00	1.00
interaction between low income indicator and female	0.35	0.00	0.48	0.00	1.00	0.36	0.00	0.48	0.00	1.00
=1 if took ntg patch continuously pre-RP	0.00	0.00	0.00	0.00	0.00	0.41	0.00	0.49	0.00	1.00
=1 if took ntg (SR)continuously pre-RP	0.00	0.00	0.00	0.00	0.00	0.61	1.00	0.49	0.00	1.00
=1 if took other restricted nitrate continuously pre-RP	0.00	0.00	0.00	0.00	0.00	0.01	0.00	0.10	0.00	1.00
=1 if took iso. dinitrate continuously pre-RP	0.99	1.00	0.11	0.00	1.00	0.00	0.00	0.00	0.00	0.00
=1 if took ntg ointment continuously pre-RP	0.02	0.00	0.14	0.00	1.00	0.00	0.00	0.00	0.00	0.00
cumulative patient payments for R drugs over post-RP period	2.26	0.00	28.55	0.00	943.44	39.16	0.00	119.99	0.00	3,607.01
=1 if total paid for R drugs > \$1	0.03	0.00	0.17	0.00	1.00	0.43	0.00	0.50	0.00	1.00
total payments for R drugs, subsample of payers > \$1	73.65	33.12	147.30	1.17	943.44	91.20	43.18	169.67	1.01	3,607.01
=1 if subject admitted to LTC facility pre RP	0.05	0.00	0.22	0.00	1.00	0.06	0.00	0.24	0.00	1.00
Length of stay: acute hospitalizations for CVD 12 months pre RP	1.22	0.00	5.44	0.00	90.00	2.46	0.00	7.41	0.00	106.00
Length of stay: Other acute care hospitalizations 12 months pre RP	1.75	0.00	6.12	0.00	76.00	2.99	0.00	9.68	0.00	172.00
Number of in-patient revascularizations 12 months pre RP	0.01	0.00	0.13	0.00	2.00	0.02	0.00	0.18	0.00	3.00
Number of other in-patient procedures 12 months pre RP	0.35	0.00	1.23	0.00	18.00	0.48	0.00	1.38	0.00	27.00
Number of Physician consultations 12 months pre RP	8.03	7.00	6.30	0.00	69.00	9.73	8.00	7.09	0.00	94.00
Number of Emergency and Hospital visits 12 months pre RP	3.26	0.00	9.08	0.00	149.00	6.11	0.00	12.73	0.00	163.00
Number of CVD Surgical Procedures 12 months pre RP	0.04	0.00	0.43	0.00	8.00	0.04	0.00	0.45	0.00	15.00
Number of CVD Diagnostic Procedures 12 months pre RP	1.50	0.00	2.55	0.00	21.00	2.25	1.00	3.32	0.00	53.00
Number of Renal Surgical & Diagnostic Procedures 12 months pre RP	0.01	0.00	0.13	0.00	2.00	0.02	0.00	0.13	0.00	3.00
Number of Renal Dialysis Procedures 12 months pre RP	0.09	0.00	3.74	0.00	157.00	0.28	0.00	6.01	0.00	208.00
Number of All other physician services 12 months pre RP	28.01	21.00	27.28	0.00	359.00	34.69	25.00	35.42	0.00	808.00

Descriptive statistics, Nitrate users, by RP exposure status, continued

Covariate Description	Unrestricted Drug User (n=1,760)					Restricted Drug User (n = 11,155)				
	Mean	Median	Std. Dev.	Min.	Max.	Mean	Median	Std. Dev.	Min.	Max.
Days supply of ACE INHIBITORS 12 months pre-RP	77.35	0.00	220.16	0.00	4,000.00	120.31	0.00	234.73	0.00	4,304.00
Days supply of CCBS 12 months pre-RP	161.45	83.00	196.80	0.00	1,400.00	192.23	150.00	219.39	0.00	2,390.00
Days supply of NITRATES 12 months pre-RP	338.96	268.00	230.04	0.00	1,560.00	427.64	377.00	220.36	0.00	2,496.00
Days supply of DIURETICS 12 months pre-RP	129.19	0.00	250.63	0.00	2,895.00	179.69	0.00	312.69	0.00	4,069.00
Days supply of ALPHA-BLOCKERS 12 months pre-RP	1.74	0.00	21.72	0.00	588.00	2.61	0.00	29.01	0.00	1,144.00
Days supply of BETA-BLOCKERS 12 months pre-RP	82.32	0.00	148.29	0.00	1,200.00	73.86	0.00	140.24	0.00	1,200.00
Days supply of AT2S 12 months pre-RP	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00
Days supply of CENTRAL ACTING & VASODILATORS 12 months pre-RP	4.17	0.00	36.75	0.00	728.00	2.76	0.00	30.15	0.00	870.00
Number of rxs of NTG SUBLINGUAL drugs 12 months pre-RP	0.72	0.00	1.30	0.00	13.00	1.10	0.00	2.02	0.00	39.00
Number of rxs of VASCULAR DISEASE drugs 12 months pre-RP	0.40	0.00	1.47	0.00	18.00	0.62	0.00	2.05	0.00	40.00
Number of rxs of EPILEPSY drugs 12 months pre-RP	0.11	0.00	0.93	0.00	21.00	0.15	0.00	1.18	0.00	53.00
Number of rxs of RHEUMATIC DISEASE drugs 12 months pre-RP	0.22	0.00	1.10	0.00	19.00	0.29	0.00	1.22	0.00	28.00
Number of rxs of HYPERCHOLESTEROLEMIA drugs 12 months pre-RP	0.50	0.00	1.47	0.00	12.00	0.52	0.00	1.52	0.00	32.00
Number of rxs of CANCER drugs 12 months pre-RP	0.02	0.00	0.37	0.00	10.00	0.03	0.00	0.42	0.00	14.00
Number of rxs of PARKINSONS DISEASE drugs 12 months pre-RP	0.09	0.00	0.91	0.00	14.00	0.07	0.00	0.91	0.00	39.00
Number of rxs of DIABETES drugs 12 months pre-RP	1.31	0.00	3.75	0.00	32.00	1.23	0.00	3.64	0.00	43.00
Number of rxs of GLAUCOMA drugs 12 months pre-RP	0.37	0.00	1.79	0.00	22.00	0.37	0.00	1.85	0.00	38.00
Number of rxs of CYSTIC FIBROSIS drugs 12 months pre-RP	0.01	0.00	0.19	0.00	6.00	0.01	0.00	0.24	0.00	12.00
Number of rxs of RESTRICTED H2RA drugs 12 months pre-RP	0.56	0.00	1.54	0.00	13.00	0.77	0.00	1.97	0.00	26.00
Number of rxs of UNRESTRICTED GI PROTECTIVE drugs 12 months pre-RP	0.58	0.00	1.72	0.00	14.00	0.81	0.00	2.08	0.00	33.00
Number of rxs of RESPIRATORY drugs 12 months pre-RP	0.81	0.00	3.14	0.00	44.00	1.12	0.00	3.93	0.00	65.00
Number of rxs of THYROID drugs 12 months pre-RP	0.53	0.00	1.68	0.00	14.00	0.60	0.00	1.79	0.00	29.00
Number of rxs of GOUT drugs 12 months pre-RP	0.31	0.00	1.25	0.00	13.00	0.25	0.00	1.10	0.00	22.00
Number of rxs of CROHN'S DISEASE drugs 12 months pre-RP	0.03	0.00	0.35	0.00	7.00	0.02	0.00	0.39	0.00	15.00
Number of rxs of RESTRICTED NSAID drugs 12 months pre-RP	0.55	0.00	1.56	0.00	13.00	0.62	0.00	1.63	0.00	16.00
Number of rxs of UNRESTRICTED NSAID drugs 12 months pre-RP	0.45	0.00	1.43	0.00	13.00	0.50	0.00	1.78	0.00	63.00
Number of rxs of PAIN drugs 12 months pre-RP	0.86	0.00	3.13	0.00	62.00	1.11	0.00	3.52	0.00	104.00
Number of rxs of ANTI-DEPRESSANT drugs 12 months pre-RP	0.39	0.00	1.49	0.00	17.00	0.60	0.00	2.12	0.00	29.00
Number of rxs of ANTI-PSYCHOSIS drugs 12 months pre-RP	0.16	0.00	1.17	0.00	18.00	0.17	0.00	1.35	0.00	43.00
Number of rxs of BIPOLAR DISORDER drugs 12 months pre-RP	0.00	0.00	0.08	0.00	3.00	0.01	0.00	0.36	0.00	25.00
Number of rxs of ANTI-ANXIETY drugs 12 months pre-RP	1.37	0.00	3.02	0.00	31.00	1.95	0.00	4.16	0.00	94.00
Number of rxs of OTHER drugs 12 months pre-RP	6.60	4.00	8.74	0.00	142.00	7.87	5.00	9.57	0.00	175.00

Descriptive statistics, Restricted Nitrate users pre-RP, by RP exposure status.

Covariate Description	Exempted (n = 2,666)			Paid (n = 3,617)			Neither (n = 4,872)		
	Mean	Median	Std. Dev.	Mean	Median	Std. Dev.	Mean	Median	Std. Dev.
age at RP of Nitrates: Nov 1, 1995	79.74	79.83	6.69	78.91	78.86	6.30	78.75	78.67	6.38
=1 if male	0.38	0.00	0.49	0.39	0.00	0.49	0.46	0.00	0.50
=1 if female	0.60	1.00	0.49	0.59	1.00	0.49	0.52	1.00	0.50
=1 if unknown sex	0.02	0.00	0.15	0.02	0.00	0.15	0.02	0.00	0.15
interaction between age and female	47.87	72.75	39.69	46.54	72.33	39.44	41.04	68.63	39.83
=1 if received MSP premium subsidy 12 months prior to RP	0.60	1.00	0.49	0.54	1.00	0.50	0.55	1.00	0.50
interaction between low income indicator and female	0.40	0.00	0.49	0.37	0.00	0.48	0.34	0.00	0.47
=1 if took ntg patch continuously pre-RP	0.45	0.00	0.50	0.40	0.00	0.49	0.39	0.00	0.49
=1 if took ntg (SR)continuously pre-RP	0.59	1.00	0.49	0.62	1.00	0.49	0.61	1.00	0.49
=1 if took other restricted nitrate continuously pre-RP	0.00	0.00	0.06	0.01	0.00	0.12	0.01	0.00	0.10
=1 if took iso. dinitrate continuously pre-RP	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00
=1 if took ntg ointment continuously pre-RP	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00
cumulative patient payments for R drugs over post-RP period	7.62	0.00	27.42	115.17	59.55	187.83	0.00	0.00	0.00
=1 if total paid for R drugs > \$1	0.44	0.00	0.50	1.00	1.00	0.02	0.00	0.00	0.00
total payments for R drugs, subsample of payers > \$1	17.29	6.42	39.26	115.20	59.56	187.84	-	-	-
=1 if subject admitted to LTC facility pre RP	0.14	0.00	0.35	0.04	0.00	0.20	0.03	0.00	0.17
Length of stay: acute care hospitalizations for CVD 12 months pre RP	2.25	0.00	7.16	2.31	0.00	6.99	2.69	0.00	7.83
Length of stay: acute care hospitalizations for Other Conditions 12 months pre RP	2.87	0.00	9.43	2.57	0.00	8.38	3.36	0.00	10.65
Number of in-patient revascularizations 12 months pre RP	0.01	0.00	0.14	0.02	0.00	0.15	0.03	0.00	0.22
Number of other in-patient procedures 12 months pre RP	0.42	0.00	1.21	0.45	0.00	1.28	0.53	0.00	1.52
Number of Physician consultations 12 months pre RP	9.33	8.00	7.06	9.96	9.00	7.20	9.77	8.00	7.02
Number of Emergency and Hospital visits 12 months pre RP	6.71	1.00	13.36	5.60	0.00	11.97	6.17	0.00	12.92
Number of CVD Surgical Procedures 12 months pre RP	0.02	0.00	0.29	0.02	0.00	0.24	0.06	0.00	0.60
Number of CVD Diagnostic Procedures 12 months pre RP	2.03	1.00	3.11	2.37	1.00	3.43	2.27	1.00	3.35
Number of Renal Surgical & Diagnostic Procedures 12 months pre RP	0.02	0.00	0.13	0.02	0.00	0.15	0.01	0.00	0.12
Number of Renal Dialysis Procedures 12 months pre RP	0.27	0.00	5.84	0.16	0.00	4.26	0.36	0.00	7.10
Number of All other physician services 12 months pre RP	35.49	26.00	33.64	34.62	25.00	36.77	34.31	24.00	35.35

Descriptive statistics, Restricted Nitrate users pre-RP, by RP exposure status, continued.

Covariate Description	Exempted (n = 2,666)			Paid (n = 3,617)			Neither (n = 4,872)		
	Mean	Median	Std. Dev.	Mean	Median	Std. Dev.	Mean	Median	Std. Dev.
Days supply of ACE INHIBITORS 12 months pre-RP	122.97	0.00	228.80	119.98	0.00	241.65	119.11	0.00	232.75
Days supply of CCBS 12 months pre-RP	197.66	168.50	218.78	191.75	150.00	216.64	189.61	142.50	221.74
Days supply of NITRATES 12 months pre-RP	462.91	416.00	238.79	429.55	380.00	224.81	406.93	373.00	203.38
Days supply of DIURETICS 12 months pre-RP	191.29	30.00	322.01	174.28	8.00	301.85	177.35	0.00	315.32
Days supply of ALPHA-BLOCKERS 12 months pre-RP	3.13	0.00	30.56	2.42	0.00	27.50	2.46	0.00	29.22
Days supply of BETA-BLOCKERS 12 months pre-RP	70.50	0.00	138.87	77.99	0.00	143.17	72.63	0.00	138.73
Days supply of AT2S 12 months pre-RP	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00
Days supply of CENTRAL ACTING and VASODILATORS 12 months pre-RP	1.76	0.00	24.23	3.20	0.00	32.02	2.98	0.00	31.60
Number of rxs of NTG SUBLINGUAL drugs 12 months pre-RP	1.22	1.00	2.16	1.13	0.00	2.11	1.02	0.00	1.86
Number of rxs of VASCULAR DISEASE drugs 12 months pre-RP	0.74	0.00	2.50	0.57	0.00	1.87	0.59	0.00	1.89
Number of rxs of EPILEPSY drugs 12 months pre-RP	0.19	0.00	1.29	0.13	0.00	0.98	0.14	0.00	1.24
Number of rxs of RHEUMATIC DISEASE drugs 12 months pre-RP	0.36	0.00	1.60	0.29	0.00	1.20	0.24	0.00	0.98
Number of rxs of HYPERCHOLESTEROLEMIA drugs 12 months pre-RP	0.57	0.00	1.56	0.48	0.00	1.46	0.53	0.00	1.53
Number of rxs of CANCER drugs 12 months pre-RP	0.04	0.00	0.53	0.02	0.00	0.32	0.04	0.00	0.42
Number of rxs of PARKINSONS DISEASE drugs 12 months pre-RP	0.09	0.00	0.96	0.06	0.00	0.88	0.07	0.00	0.91
Number of rxs of DIABETES drugs 12 months pre-RP	1.20	0.00	3.72	1.22	0.00	3.67	1.25	0.00	3.58
Number of rxs of GLAUCOMA drugs 12 months pre-RP	0.46	0.00	2.17	0.36	0.00	1.73	0.34	0.00	1.75
Number of rxs of CYSTIC FIBROSIS drugs 12 months pre-RP	0.00	0.00	0.10	0.02	0.00	0.35	0.01	0.00	0.19
Number of rxs of RESTRICTED H2RA drugs 12 months pre-RP	0.94	0.00	2.26	0.74	0.00	2.02	0.70	0.00	1.75
Number of rxs of UNRESTRICTED GI PROTECTIVE drugs 12 months pre-RP	0.98	0.00	2.39	0.80	0.00	2.06	0.72	0.00	1.90
Number of rxs of RESPIRATORY drugs 12 months pre-RP	1.22	0.00	4.15	1.16	0.00	4.11	1.03	0.00	3.67
Number of rxs of THYROID drugs 12 months pre-RP	0.75	0.00	2.16	0.58	0.00	1.79	0.53	0.00	1.56
Number of rxs of GOUT drugs 12 months pre-RP	0.26	0.00	1.22	0.26	0.00	1.11	0.24	0.00	1.01
Number of rxs of CROHN'S DISEASE drugs 12 months pre-RP	0.03	0.00	0.53	0.02	0.00	0.31	0.02	0.00	0.36
Number of rxs of RESTRICTED NSAID drugs 12 months pre-RP	0.66	0.00	1.75	0.63	0.00	1.67	0.60	0.00	1.54
Number of rxs of UNRESTRICTED NSAID drugs 12 months pre-RP	0.82	0.00	2.61	0.43	0.00	1.55	0.39	0.00	1.29
Number of rxs of PAIN drugs 12 months pre-RP	1.25	0.00	3.85	1.08	0.00	3.41	1.06	0.00	3.41
Number of rxs of ANTI-DEPRESSANT drugs 12 months pre-RP	0.79	0.00	2.61	0.51	0.00	1.90	0.57	0.00	1.96
Number of rxs of ANTI-PSYCHOSIS drugs 12 months pre-RP	0.34	0.00	2.07	0.12	0.00	1.13	0.11	0.00	0.95
Number of rxs of BIPOLAR DISORDER drugs 12 months pre-RP	0.01	0.00	0.24	0.02	0.00	0.52	0.01	0.00	0.27
Number of rxs of ANTI-ANXIETY drugs 12 months pre-RP	2.26	0.00	4.21	1.99	0.00	4.20	1.74	0.00	4.09
Number of rxs of OTHER drugs 12 months pre-RP	9.57	6.00	11.80	7.81	5.00	9.19	6.99	5.00	8.27

Descriptive statistics, ACE inhibitor users, by RP exposure status.

Covariate Description	Restricted Drug User (n= 28,564)					Unrestricted Drug User (n = 7,320)				
	Mean	Median	Std. Dev.	Min.	Max.	Std. Dev.	Median	Std. Dev.	Min.	Max.
age at RP of ACE/CCB: Jan 1, 1997	76.62	75.72	6.69	65.51	107.84	77.41	76.63	6.83	65.55	105.33
=1 if male	0.40	0.00	0.49	0.00	1.00	0.39	0.00	0.49	0.00	1.00
=1 if female	0.58	1.00	0.49	0.00	1.00	0.59	1.00	0.49	0.00	1.00
=1 if unknown sex	0.02	0.00	0.13	0.00	1.00	0.02	0.00	0.14	0.00	1.00
interaction between age and female	44.66	69.67	38.47	0.00	102.91	46.03	70.59	38.80	0.00	102.32
=1 if received MSP premium subsidy 12 months prior to RP	0.46	0.00	0.50	0.00	1.00	0.46	0.00	0.50	0.00	1.00
interaction between low income indicator and female	0.31	0.00	0.46	0.00	1.00	0.32	0.00	0.47	0.00	1.00
=1 if took enalapril continuously pre-RP	0.70	1.00	0.46	0.00	1.00	0.00	0.00	0.00	0.00	0.00
=1 if took lisinopril continuously pre-RP	0.22	0.00	0.41	0.00	1.00	0.00	0.00	0.00	0.00	0.00
=1 if took fosinopril continuously pre-RP	0.04	0.00	0.20	0.00	1.00	0.00	0.00	0.00	0.00	0.00
=1 if took cilazapril continuously pre-RP	0.03	0.00	0.18	0.00	1.00	0.00	0.00	0.00	0.00	0.00
=1 if took benazepril continuously pre-RP	0.01	0.00	0.11	0.00	1.00	0.00	0.00	0.00	0.00	0.00
=1 if took captopril continuously pre-RP	0.00	0.00	0.00	0.00	0.00	0.66	1.00	0.47	0.00	1.00
=1 if took quinapril continuously pre-RP	0.00	0.00	0.00	0.00	0.00	0.15	0.00	0.36	0.00	1.00
=1 if took ramipril continuously pre-RP	0.00	0.00	0.00	0.00	0.00	0.19	0.00	0.39	0.00	1.00
* cumulative patient payments for R drugs over RP period	53.98	5.59	140.04	0.00	6290.86	2.31	0.00	26.28	0.00	863.44
=1 if total paid for R drugs > \$1	0.56	1.00	0.50	0.00	1.00	0.03	0.00	0.17	0.00	1.00
total payments for R drugs, subsample of payers > \$1	96.18	40.55	175.74	1.01	6290.86	77.73	26.90	131.94	1.01	863.44
=1 if subject admitted to LTC facility pre RP	0.04	0.00	0.20	0.00	1.00	0.05	0.00	0.22	0.00	1.00
Length of stay: acute hospitalizations for CVD 12 months pre RP	0.19	0.00	2.31	0.00	118.00	0.25	0.00	2.71	0.00	87.00
Length of stay: acute hospitalizations for Other Conditions 12 months pre RP	0.73	0.00	4.86	0.00	155.00	0.87	0.00	5.20	0.00	107.00
Number of in-patient revascularizations 12 months pre RP	0.00	0.00	0.05	0.00	2.00	0.00	0.00	0.06	0.00	2.00
Number of other in-patient procedures 12 months pre RP	0.10	0.00	0.60	0.00	17.00	0.11	0.00	0.66	0.00	22.00
Number of Physician consultations 12 months pre RP	7.19	6.00	5.55	0.00	87.00	7.24	6.00	5.63	0.00	61.00
Number of Emergency and Hospital visits 12 months pre RP	3.29	0.00	9.23	0.00	144.00	3.71	0.00	9.86	0.00	156.00
Number of CVD Surgical Procedures 12 months pre RP	0.04	0.00	0.43	0.00	20.00	0.03	0.00	0.31	0.00	10.00
Number of CVD Diagnostic Procedures 12 months pre RP	1.37	0.00	2.59	0.00	37.00	1.35	0.00	2.51	0.00	25.00
Number of Renal Surgical & Diagnostic Procedures 12 months pre RP	0.01	0.00	0.13	0.00	4.00	0.01	0.00	0.13	0.00	4.00
Number of Renal Dialysis Procedures 12 months pre RP	0.02	0.00	1.62	0.00	157.00	0.04	0.00	2.55	0.00	154.00
Number of All other physician services 12 months pre RP	30.17	21.00	30.77	0.00	572.00	31.16	22.00	32.47	0.00	621.00

Descriptive statistics, ACE inhibitor users, by RP exposure status, continued.

Covariate Description	Restricted Drug User (n= 28,564)					Unrestricted Drug User (n = 7,320)				
	Mean	Median	Std. Dev.	Min.	Max.	Std. Dev.	Median	Std. Dev.	Min.	Max.
Days supply of ACE INHIBITORS 12 months pre-RP	391.64	304.00	285.96	0.00	3200.00	476.30	366.00	376.74	0.00	3600.00
Days supply of CCBS 12 months pre-RP	15.16	0.00	67.72	0.00	1880.00	16.11	0.00	66.02	0.00	1500.00
Days supply of NITRATES 12 months pre-RP	27.34	0.00	105.84	0.00	2048.00	36.03	0.00	117.79	0.00	1397.00
Days supply of DIURETICS 12 months pre-RP	146.49	0.00	251.31	0.00	4650.00	194.69	75.00	304.50	0.00	5181.00
Days supply of ALPHA-BLOCKERS 12 months pre-RP	4.49	0.00	42.96	0.00	1600.00	4.94	0.00	45.30	0.00	1600.00
Days supply of BETA-BLOCKERS 12 months pre-RP	37.34	0.00	113.88	0.00	2760.00	38.91	0.00	112.75	0.00	1067.00
Days supply of AT2S 12 months pre-RP	0.05	0.00	2.19	0.00	180.00	0.03	0.00	1.68	0.00	100.00
Days supply of CENTRAL ACTING & VASODILATORS 12 months pre-RP	1.65	0.00	22.68	0.00	940.00	3.26	0.00	35.87	0.00	1080.00
Number of rxs of NTG SUBLINGUAL drugs 12 months pre-RP	0.18	0.00	0.76	0.00	24.00	0.22	0.00	0.93	0.00	31.00
Number of rxs of VASCULAR DISEASE drugs 12 months pre-RP	0.58	0.00	2.11	0.00	101.00	0.59	0.00	1.96	0.00	51.00
Number of rxs of EPILEPSY drugs 12 months pre-RP	0.12	0.00	1.00	0.00	46.00	0.14	0.00	1.25	0.00	50.00
Number of rxs of RHEUMATIC DISEASE drugs 12 months pre-RP	0.22	0.00	1.08	0.00	32.00	0.24	0.00	1.25	0.00	49.00
Number of rxs of HYPERCHOLESTEROLEMIA drugs 12 months pre-RP	0.39	0.00	1.31	0.00	35.00	0.42	0.00	1.45	0.00	51.00
Number of rxs of CANCER drugs 12 months pre-RP	0.03	0.00	0.37	0.00	14.00	0.02	0.00	0.30	0.00	10.00
Number of rxs of PARKINSONS DISEASE drugs 12 months pre-RP	0.05	0.00	0.70	0.00	32.00	0.06	0.00	0.73	0.00	17.00
Number of rxs of DIABETES drugs 12 months pre-RP	1.08	0.00	3.34	0.00	52.00	1.28	0.00	3.85	0.00	97.00
Number of rxs of GLAUCOMA drugs 12 months pre-RP	0.36	0.00	1.87	0.00	53.00	0.38	0.00	1.87	0.00	34.00
Number of rxs of CYSTIC FIBROSIS drugs 12 months pre-RP	0.01	0.00	0.24	0.00	15.00	0.01	0.00	0.19	0.00	10.00
Number of rxs of RESTRICTED H2RA drugs 12 months pre-RP	0.19	0.00	0.99	0.00	40.00	0.21	0.00	1.28	0.00	48.00
Number of rxs of UNRESTRICTED GI PROTECTIVE drugs 12 months pre-RP	0.63	0.00	1.89	0.00	85.00	0.64	0.00	2.02	0.00	64.00
Number of rxs of RESPIRATORY drugs 12 months pre-RP	0.88	0.00	3.60	0.00	130.00	1.01	0.00	3.87	0.00	61.00
Number of rxs of THYROID drugs 12 months pre-RP	0.52	0.00	1.69	0.00	53.00	0.55	0.00	1.92	0.00	51.00
Number of rxs of GOUT drugs 12 months pre-RP	0.22	0.00	1.09	0.00	53.00	0.26	0.00	1.24	0.00	51.00
Number of rxs of CROHN'S DISEASE drugs 12 months pre-RP	0.02	0.00	0.32	0.00	16.00	0.02	0.00	0.34	0.00	11.00
Number of rxs of RESTRICTED NSAID drugs 12 months pre-RP	0.28	0.00	1.04	0.00	22.00	0.28	0.00	1.13	0.00	34.00
Number of rxs of UNRESTRICTED NSAID drugs 12 months pre-RP	0.50	0.00	1.63	0.00	53.00	0.50	0.00	1.53	0.00	17.00
Number of rxs of PAIN drugs 12 months pre-RP	0.78	0.00	2.73	0.00	97.00	0.73	0.00	2.48	0.00	36.00
Number of rxs of ANTI-DEPRESSANT drugs 12 months pre-RP	0.52	0.00	1.92	0.00	51.00	0.55	0.00	2.05	0.00	50.00
Number of rxs of ANTI-PSYCHOSIS drugs 12 months pre-RP	0.13	0.00	1.19	0.00	53.00	0.13	0.00	1.14	0.00	50.00
Number of rxs of BIPOLAR DISORDER drugs 12 months pre-RP	0.01	0.00	0.43	0.00	52.00	0.01	0.00	0.26	0.00	11.00
Number of rxs of ANTI-ANXIETY drugs 12 months pre-RP	1.22	0.00	3.19	0.00	99.00	1.37	0.00	3.31	0.00	51.00
Number of rxs of OTHER drugs 12 months pre-RP	5.86	3.00	8.04	0.00	101.00	6.80	4.00	9.39	0.00	164.00

Descriptive statistics, Restricted ACE inhibitor users pre-RP, by RP exposure status.

Covariate Description	Exempted (n = 15,110)			Paid (n = 9,262)			Neither (n= 4,191)		
	Mean	Median	Std. Dev.	Mean	Median	Std. Dev.	Mean	Median	Std. Dev.
age at RP of ACE/CCB: Jan 1, 1997	76.44	75.46	6.65	76.72	75.84	6.71	77.05	76.33	6.78
=1 if male	0.42	0.00	0.49	0.38	0.00	0.49	0.42	0.00	0.49
=1 if female	0.57	1.00	0.50	0.60	1.00	0.49	0.56	1.00	0.50
=1 if unknown sex	0.02	0.00	0.13	0.02	0.00	0.13	0.02	0.00	0.14
interaction between age and female	43.77	69.17	38.47	46.55	70.66	38.30	43.73	69.17	38.72
=1 if received MSP premium subsidy 12 months prior to RP	0.46	0.00	0.50	0.44	0.00	0.50	0.50	0.00	0.50
interaction between low income indicator and female	0.31	0.00	0.46	0.31	0.00	0.46	0.32	0.00	0.47
=1 if took enalapril continuously pre-RP	0.67	1.00	0.47	0.72	1.00	0.45	0.72	1.00	0.45
=1 if took lisinopril continuously pre-RP	0.24	0.00	0.42	0.19	0.00	0.40	0.21	0.00	0.40
=1 if took fosinopril continuously pre-RP	0.04	0.00	0.19	0.05	0.00	0.21	0.04	0.00	0.21
=1 if took cilazapril continuously pre-RP	0.04	0.00	0.19	0.03	0.00	0.17	0.03	0.00	0.16
=1 if took benazepril continuously pre-RP	0.01	0.00	0.12	0.01	0.00	0.10	0.01	0.00	0.09
=1 if took captopril continuously pre-RP	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00
=1 if took quinapril continuously pre-RP	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00
=1 if took ramipril continuously pre-RP	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00
* cumulative patient payments for R drugs over RP period	8.18	0.00	20.07	153.15	89.46	212.72	0.00	0.00	0.00
=1 if total paid for R drugs > \$1	0.45	0.00	0.50	1.00	1.00	0.00	0.00	0.00	0.00
total payments for R drugs, subsample of payers > \$1	18.25	13.72	26.74	153.15	89.46	212.72	-	-	-
=1 if subject admitted to LTC facility pre RP	0.04	0.00	0.20	0.04	0.00	0.18	0.06	0.00	0.24
Length of stay: acute hospitalizations for CVD 12 months pre RP	0.14	0.00	1.66	0.19	0.00	2.30	0.37	0.00	3.84
Length of stay: acute hospitalizations for Other Conditions 12 months pre RP	0.70	0.00	4.58	0.57	0.00	4.55	1.20	0.00	6.28
Number of in-patient revascularizations 12 months pre RP	0.00	0.00	0.03	0.00	0.00	0.06	0.00	0.00	0.05
Number of other in-patient procedures 12 months pre RP	0.09	0.00	0.56	0.09	0.00	0.55	0.14	0.00	0.81
Number of Physician consultations 12 months pre RP	7.17	6.00	5.58	7.12	6.00	5.44	7.44	6.00	5.64
Number of Emergency and Hospital visits 12 months pre RP	3.10	0.00	8.73	2.82	0.00	8.27	5.03	0.00	12.28
Number of CVD Surgical Procedures 12 months pre RP	0.03	0.00	0.43	0.04	0.00	0.48	0.03	0.00	0.30
Number of CVD Diagnostic Procedures 12 months pre RP	1.28	0.00	2.43	1.52	0.00	2.80	1.37	0.00	2.68
Number of Renal Surgical & Diagnostic Procedures 12 months pre RP	0.01	0.00	0.12	0.01	0.00	0.11	0.02	0.00	0.16
Number of Renal Dialysis Procedures 12 months pre RP	0.03	0.00	1.82	0.00	0.00	0.05	0.05	0.00	2.45
Number of All other physician services 12 months pre RP	30.29	22.00	30.62	29.38	21.00	29.75	31.51	22.00	33.39

Descriptive statistics, Restricted ACE inhibitor users pre-RP, by RP exposure status, continued.

Covariate Description	Exempted (n = 15,110)			Paid (n = 9,262)			Neither (n= 4,191)		
	Mean	Median	Std. Dev.	Mean	Median	Std. Dev.	Mean	Median	Std. Dev.
Days supply of ACE INHIBITORS 12 months pre-RP	325.82	268.00	240.69	485.77	400.00	318.09	420.92	350.00	298.05
Days supply of CCBS 12 months pre-RP	14.01	0.00	67.80	14.73	0.00	64.69	20.24	0.00	73.51
Days supply of NITRATES 12 months pre-RP	26.75	0.00	105.15	27.52	0.00	106.01	29.07	0.00	107.97
Days supply of DIURETICS 12 months pre-RP	142.57	0.00	253.31	146.63	0.00	244.75	160.29	30.00	257.88
Days supply of ALPHA-BLOCKERS 12 months pre-RP	4.11	0.00	42.34	5.21	0.00	46.12	4.25	0.00	37.61
Days supply of BETA-BLOCKERS 12 months pre-RP	30.11	0.00	99.66	49.08	0.00	133.89	37.43	0.00	111.66
Days supply of AT2S 12 months pre-RP	0.01	0.00	1.09	0.02	0.00	1.33	0.25	0.00	4.93
Days supply of CENTRAL ACTING & VASODILATORS 12 months pre-RP	1.40	0.00	21.14	1.84	0.00	22.42	2.14	0.00	27.96
Number of rxs of NTG SUBLINGUAL drugs 12 months pre-RP	0.17	0.00	0.72	0.18	0.00	0.78	0.21	0.00	0.87
Number of rxs of VASCULAR DISEASE drugs 12 months pre-RP	0.57	0.00	2.07	0.62	0.00	2.27	0.54	0.00	1.89
Number of rxs of EPILEPSY drugs 12 months pre-RP	0.12	0.00	0.87	0.11	0.00	1.16	0.14	0.00	1.05
Number of rxs of RHEUMATIC DISEASE drugs 12 months pre-RP	0.25	0.00	1.14	0.17	0.00	0.98	0.24	0.00	1.08
Number of rxs of HYPERCHOLESTEROLEMIA drugs 12 months pre-RP	0.40	0.00	1.35	0.40	0.00	1.32	0.32	0.00	1.09
Number of rxs of CANCER drugs 12 months pre-RP	0.03	0.00	0.37	0.02	0.00	0.37	0.03	0.00	0.38
Number of rxs of PARKINSONS DISEASE drugs 12 months pre-RP	0.05	0.00	0.66	0.05	0.00	0.74	0.05	0.00	0.72
Number of rxs of DIABETES drugs 12 months pre-RP	1.69	0.00	4.03	0.10	0.00	1.03	1.06	0.00	3.42
Number of rxs of GLAUCOMA drugs 12 months pre-RP	0.37	0.00	1.89	0.36	0.00	1.90	0.32	0.00	1.72
Number of rxs of CYSTIC FIBROSIS drugs 12 months pre-RP	0.01	0.00	0.28	0.01	0.00	0.21	0.01	0.00	0.13
Number of rxs of RESTRICTED H2RA drugs 12 months pre-RP	0.20	0.00	1.07	0.16	0.00	0.86	0.18	0.00	0.93
Number of rxs of UNRESTRICTED GI PROTECTIVE drugs 12 months pre-RP	0.64	0.00	1.84	0.61	0.00	2.05	0.61	0.00	1.70
Number of rxs of RESPIRATORY drugs 12 months pre-RP	1.35	0.00	4.46	0.13	0.00	1.13	0.83	0.00	3.43
Number of rxs of THYROID drugs 12 months pre-RP	0.54	0.00	1.77	0.50	0.00	1.60	0.48	0.00	1.58
Number of rxs of GOUT drugs 12 months pre-RP	0.23	0.00	1.19	0.20	0.00	0.95	0.21	0.00	0.98
Number of rxs of CROHN'S DISEASE drugs 12 months pre-RP	0.02	0.00	0.33	0.02	0.00	0.34	0.01	0.00	0.22
Number of rxs of RESTRICTED NSAID drugs 12 months pre-RP	0.27	0.00	1.02	0.30	0.00	1.11	0.26	0.00	0.98
Number of rxs of UNRESTRICTED NSAID drugs 12 months pre-RP	0.52	0.00	1.72	0.47	0.00	1.51	0.51	0.00	1.55
Number of rxs of PAIN drugs 12 months pre-RP	0.79	0.00	2.75	0.74	0.00	2.71	0.87	0.00	2.69
Number of rxs of ANTI-DEPRESSANT drugs 12 months pre-RP	0.52	0.00	1.92	0.51	0.00	1.91	0.57	0.00	1.98
Number of rxs of ANTI-PSYCHOSIS drugs 12 months pre-RP	0.13	0.00	1.17	0.11	0.00	1.17	0.16	0.00	1.29
Number of rxs of BIPOLAR DISORDER drugs 12 months pre-RP	0.01	0.00	0.49	0.01	0.00	0.25	0.01	0.00	0.49
Number of rxs of ANTI-ANXIETY drugs 12 months pre-RP	1.18	0.00	3.19	1.25	0.00	3.18	1.29	0.00	3.22
Number of rxs of OTHER drugs 12 months pre-RP	6.34	4.00	8.38	4.96	3.00	7.10	6.12	4.00	8.55

Descriptive statistics, CCB users, by RP exposure status.

Covariate Description	Restricted (n = 14,342)					Unrestricted (n = 20,086)				
	Mean	Median	Std. Dev.	Min.	Max.	Mean	Median	Std. Dev.	Min.	Max.
age at RP of ACE/CCB: Jan 1, 1997	76.61	75.86	6.27	65.54	100.96	77.15	76.42	6.20	65.55	100.50
=1 if male	0.40	0.00	0.49	0.00	1.00	0.38	0.00	0.49	0.00	1.00
=1 if female	0.59	1.00	0.49	0.00	1.00	0.60	1.00	0.49	0.00	1.00
=1 if unknown sex	0.01	0.00	0.12	0.00	1.00	0.02	0.00	0.12	0.00	1.00
interaction between age and female	45.48	70.46	38.23	0.00	100.96	46.64	71.27	38.25	0.00	100.33
=1 if received MSP premium subsidy 12 months prior to RP	0.48	0.00	0.50	0.00	1.00	0.47	0.00	0.50	0.00	1.00
interaction between low income indicator and female	0.33	0.00	0.47	0.00	1.00	0.33	0.00	0.47	0.00	1.00
=1 if took nifedipine continuously pre-RP	0.03	0.00	0.17	0.00	1.00	0.00	0.00	0.00	0.00	0.00
=1 if took nifedipine (SR) continuously pre-RP	0.71	1.00	0.45	0.00	1.00	0.00	0.00	0.00	0.00	0.00
=1 if took nicardipine continuously pre-RP	0.01	0.00	0.10	0.00	1.00	0.00	0.00	0.00	0.00	0.00
=1 if took amlodipine continuously pre-RP	0.25	0.00	0.43	0.00	1.00	0.00	0.00	0.00	0.00	0.00
=1 if took felodipine continuously pre-RP	0.00	0.00	0.00	0.00	0.00	0.09	0.00	0.29	0.00	1.00
=1 if took diltiazem continuously pre-RP	0.00	0.00	0.00	0.00	0.00	0.55	1.00	0.50	0.00	1.00
=1 if took diltiazem (SR) continuously pre-RP	0.00	0.00	0.00	0.00	0.00	0.04	0.00	0.20	0.00	1.00
=1 if took verapamil continuously pre-RP	0.00	0.00	0.00	0.00	0.00	0.16	0.00	0.36	0.00	1.00
* cumulative patient payments for R drugs over RP period	21.80	0.00	56.11	0.00	971.27	1.04	0.00	12.68	0.00	675.82
=1 if total paid for R drugs > \$1	0.43	0.00	0.49	0.00	1.00	0.02	0.00	0.14	0.00	1.00
total payments for R drugs, subsample of payers > \$1	51.18	24.09	76.73	1.02	971.27	52.29	26.18	73.36	1.03	675.82
=1 if subject admitted to LTC facility pre RP	0.03	0.00	0.17	0.00	1.00	0.03	0.00	0.18	0.00	1.00
Length of stay: acute care hospitalizations for CVD 12 months pre RP	0.73	0.00	4.28	0.00	125.00	0.70	0.00	3.96	0.00	157.00
Length of stay: acute care hospitalizations for Other Conditions 12 months pre RP	1.54	0.00	6.29	0.00	135.00	1.94	0.00	7.76	0.00	151.00
Number of in-patient revascularizations 12 months pre RP	0.01	0.00	0.15	0.00	4.00	0.02	0.00	0.18	0.00	7.00
Number of other in-patient procedures 12 months pre RP	0.26	0.00	0.95	0.00	18.00	0.27	0.00	0.94	0.00	14.00
Number of Physician consultations 12 months pre RP	6.92	6.00	5.27	0.00	80.00	7.04	6.00	5.42	0.00	118.00
Number of Emergency and Hospital visits 12 months pre RP	2.25	0.00	7.03	0.00	147.00	2.67	0.00	8.07	0.00	192.00
Number of CVD Surgical Procedures 12 months pre RP	0.03	0.00	0.29	0.00	10.00	0.03	0.00	0.35	0.00	16.00
Number of CVD Diagnostic Procedures 12 months pre RP	1.22	0.00	2.32	0.00	28.00	1.49	0.00	2.54	0.00	30.00
Number of Renal Surgical & Diagnostic Procedures 12 months pre RP	0.02	0.00	0.16	0.00	4.00	0.02	0.00	0.14	0.00	5.00
Number of Renal Dialysis Procedures 12 months pre RP	0.09	0.00	3.10	0.00	157.00	0.07	0.00	3.02	0.00	157.00
Number of All other physician services 12 months pre RP	27.34	19.00	31.19	0.00	680.00	28.96	21.00	29.23	0.00	785.00

Descriptive statistics, CCB users, by RP exposure status, continued.

Covariate Description	Restricted (n = 14,342)					Unrestricted (n = 20,086)				
	Mean	Median	Std. Dev.	Min.	Max.	Mean	Median	Std. Dev.	Min.	Max.
Days supply of ACE INHIBITORS 12 months pre-RP	16.08	0.00	85.69	0.00	2400.00	12.86	0.00	65.42	0.00	1710.00
Days supply of CCBS 12 months pre-RP	424.95	385.50	184.21	0.00	2340.00	319.95	300.00	163.51	0.00	2160.00
Days supply of NITRATES 12 months pre-RP	41.57	0.00	136.00	0.00	1744.00	68.72	0.00	168.09	0.00	2172.00
Days supply of DIURETICS 12 months pre-RP	75.32	0.00	163.48	0.00	2719.00	77.68	0.00	164.55	0.00	3000.00
Days supply of ALPHA-BLOCKERS 12 months pre-RP	4.27	0.00	38.81	0.00	1560.00	4.79	0.00	44.91	0.00	1600.00
Days supply of BETA-BLOCKERS 12 months pre-RP	60.02	0.00	134.77	0.00	1335.00	32.76	0.00	100.53	0.00	1440.00
Days supply of AT2S 12 months pre-RP	0.14	0.00	4.52	0.00	380.00	0.18	0.00	4.76	0.00	300.00
Days supply of CENTRAL ACTING and VASODILATORS 12 months pre-RP	1.57	0.00	22.24	0.00	700.00	1.68	0.00	23.05	0.00	900.00
Number of rxs of NTG SUBLINGUAL drugs 12 months pre-RP	0.24	0.00	0.85	0.00	20.00	0.37	0.00	1.02	0.00	24.00
Number of rxs of VASCULAR DISEASE drugs 12 months pre-RP	0.39	0.00	1.67	0.00	61.00	0.47	0.00	1.78	0.00	52.00
Number of rxs of EPILEPSY drugs 12 months pre-RP	0.11	0.00	0.92	0.00	33.00	0.12	0.00	1.06	0.00	53.00
Number of rxs of RHEUMATIC DISEASE drugs 12 months pre-RP	0.20	0.00	0.96	0.00	19.00	0.23	0.00	1.07	0.00	30.00
Number of rxs of HYPERCHOLESTEROLEMIA drugs 12 months pre-RP	0.54	0.00	1.54	0.00	36.00	0.61	0.00	1.54	0.00	26.00
Number of rxs of CANCER drugs 12 months pre-RP	0.03	0.00	0.51	0.00	26.00	0.03	0.00	0.40	0.00	14.00
Number of rxs of PARKINSONS DISEASE drugs 12 months pre-RP	0.05	0.00	0.70	0.00	30.00	0.05	0.00	0.72	0.00	34.00
Number of rxs of DIABETES drugs 12 months pre-RP	0.87	0.00	2.87	0.00	63.00	0.87	0.00	3.04	0.00	80.00
Number of rxs of GLAUCOMA drugs 12 months pre-RP	0.37	0.00	1.82	0.00	31.00	0.36	0.00	1.80	0.00	49.00
Number of rxs of CYSTIC FIBROSIS drugs 12 months pre-RP	0.01	0.00	0.24	0.00	15.00	0.01	0.00	0.22	0.00	13.00
Number of rxs of RESTRICTED H2RA drugs 12 months pre-RP	0.21	0.00	1.06	0.00	33.00	0.23	0.00	1.14	0.00	44.00
Number of rxs of UNRESTRICTED GI PROTECTIVE drugs 12 months pre-RP	0.70	0.00	1.93	0.00	48.00	0.78	0.00	1.92	0.00	38.00
Number of rxs of RESPIRATORY drugs 12 months pre-RP	0.71	0.00	2.96	0.00	65.00	0.91	0.00	3.40	0.00	75.00
Number of rxs of THYROID drugs 12 months pre-RP	0.49	0.00	1.59	0.00	50.00	0.53	0.00	1.67	0.00	50.00
Number of rxs of GOUT drugs 12 months pre-RP	0.19	0.00	0.90	0.00	26.00	0.16	0.00	0.87	0.00	26.00
Number of rxs of CROHN'S DISEASE drugs 12 months pre-RP	0.02	0.00	0.48	0.00	36.00	0.02	0.00	0.36	0.00	18.00
Number of rxs of RESTRICTED NSAID drugs 12 months pre-RP	0.31	0.00	1.18	0.00	30.00	0.30	0.00	1.13	0.00	38.00
Number of rxs of UNRESTRICTED NSAID drugs 12 months pre-RP	0.55	0.00	1.64	0.00	48.00	0.55	0.00	1.61	0.00	53.00
Number of rxs of PAIN drugs 12 months pre-RP	0.68	0.00	2.51	0.00	100.00	0.77	0.00	2.57	0.00	81.00
Number of rxs of ANTI-DEPRESSANT drugs 12 months pre-RP	0.50	0.00	2.05	0.00	48.00	0.53	0.00	2.08	0.00	54.00
Number of rxs of ANTI-PSYCHOSIS drugs 12 months pre-RP	0.11	0.00	1.03	0.00	42.00	0.12	0.00	1.22	0.00	50.00
Number of rxs of BIPOLAR DISORDER drugs 12 months pre-RP	0.01	0.00	0.33	0.00	16.00	0.01	0.00	0.43	0.00	48.00
Number of rxs of ANTI-ANXIETY drugs 12 months pre-RP	1.24	0.00	3.22	0.00	85.00	1.34	0.00	3.24	0.00	88.00
Number of rxs of OTHER drugs 12 months pre-RP	4.83	3.00	6.76	0.00	91.00	5.52	3.00	7.66	0.00	142.00

Descriptive statistics, Restricted CCB users pre-RP, by RP exposure status.

Covariate Description	Exempted (n = 8,886)			Paid (n = 3,445)			Neither (n = 2,011)		
	Mean	Median	Std. Dev.	Mean	Median	Std. Dev.	Mean	Median	Std. Dev.
age at RP of ACE/CCB: Jan 1, 1997	76.38	75.67	6.20	76.89	76.17	6.22	77.15	76.47	6.60
=1 if male	0.39	0.00	0.49	0.39	0.00	0.49	0.41	0.00	0.49
=1 if female	0.59	1.00	0.49	0.59	1.00	0.49	0.57	1.00	0.49
=1 if unknown sex	0.01	0.00	0.11	0.02	0.00	0.13	0.02	0.00	0.13
interaction between age and female	45.57	70.42	38.04	45.90	70.84	38.43	44.38	69.82	38.70
=1 if received MSP premium subsidy 12 months prior to RP	0.48	0.00	0.50	0.47	0.00	0.50	0.50	1.00	0.50
interaction between low income indicator and female	0.33	0.00	0.47	0.32	0.00	0.47	0.34	0.00	0.47
=1 if took nifedipine continuously pre-RP	0.02	0.00	0.14	0.02	0.00	0.14	0.08	0.00	0.27
=1 if took nifedipine (SR)continuously pre-RP	0.69	1.00	0.46	0.89	1.00	0.31	0.53	1.00	0.50
=1 if took nicardipine continuously pre-RP	0.01	0.00	0.09	0.01	0.00	0.12	0.01	0.00	0.10
=1 if took amlodipine continuously pre-RP	0.29	0.00	0.45	0.08	0.00	0.27	0.38	0.00	0.48
=1 if took felodipine continuously pre-RP	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00
=1 if took diltiazem continuously pre-RP	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00
=1 if took diltiazem (SR) continuously pre-RP	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00
=1 if took verapamil continuously pre-RP	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00
* cumulative patient payments for R drugs over RP period	12.83	0.00	38.17	57.66	26.04	87.05	0.00	0.00	0.00
=1 if total paid for R drugs > \$1	0.32	0.00	0.47	0.95	1.00	0.22	0.00	0.00	0.00
total payments for R drugs, subsample of payers > \$1	40.03	14.00	58.80	60.91	27.10	88.36	-	-	-
=1 if subject admitted to LTC facility pre RP	0.02	0.00	0.15	0.04	0.00	0.19	0.05	0.00	0.22
Length of stay: acute care hospitalizations for CVD 12 months pre RP	0.63	0.00	3.83	0.52	0.00	3.82	1.49	0.00	6.37
Length of stay: acute care hospitalizations for Other Conditions 12 months pre RP	1.32	0.00	5.45	1.58	0.00	6.50	2.44	0.00	8.83
Number of in-patient revascularizations 12 months pre RP	0.01	0.00	0.15	0.00	0.00	0.09	0.03	0.00	0.22
Number of other in-patient procedures 12 months pre RP	0.24	0.00	0.90	0.27	0.00	0.97	0.37	0.00	1.12
Number of Physician consultations 12 months pre RP	6.97	6.00	5.27	6.70	6.00	5.17	7.08	6.00	5.41
Number of Emergency and Hospital visits 12 months pre RP	2.01	0.00	6.61	2.03	0.00	6.14	3.66	0.00	9.63
Number of CVD Surgical Procedures 12 months pre RP	0.02	0.00	0.28	0.01	0.00	0.18	0.06	0.00	0.42
Number of CVD Diagnostic Procedures 12 months pre RP	1.25	0.00	2.35	1.06	0.00	2.08	1.33	0.00	2.51
Number of Renal Surgical & Diagnostic Procedures 12 months pre RP	0.02	0.00	0.15	0.02	0.00	0.17	0.02	0.00	0.16
Number of Renal Dialysis Procedures 12 months pre RP	0.09	0.00	3.24	0.08	0.00	2.99	0.10	0.00	2.65
Number of All other physician services 12 months pre RP	27.32	19.00	31.15	26.49	19.00	30.17	28.87	19.00	33.02

Descriptive statistics, Restricted CCB users pre-RP, by RP exposure status, continued

Covariate Description	Exempted (n = 8,886)			Paid (n = 3,445)			Neither (n = 2,011)		
	Mean	Median	Std. Dev.	Mean	Median	Std. Dev.	Mean	Median	Std. Dev.
Days supply of ACE INHIBITORS 12 months pre-RP	16.01	0.00	86.05	13.50	0.00	83.79	20.82	0.00	87.16
Days supply of CCBS 12 months pre-RP	414.46	380.00	171.35	447.46	390.00	196.92	432.69	390.00	210.87
Days supply of NITRATES 12 months pre-RP	41.58	0.00	133.53	41.39	0.00	139.30	41.82	0.00	141.05
Days supply of DIURETICS 12 months pre-RP	75.10	0.00	165.72	72.34	0.00	155.08	81.41	0.00	167.41
Days supply of ALPHA-BLOCKERS 12 months pre-RP	3.77	0.00	35.64	5.04	0.00	38.54	5.17	0.00	50.83
Days supply of BETA-BLOCKERS 12 months pre-RP	59.60	0.00	133.78	67.03	0.00	144.97	49.88	0.00	119.53
Days supply of AT2S 12 months pre-RP	0.11	0.00	3.11	0.12	0.00	3.70	0.30	0.00	8.91
Days supply of CENTRAL ACTING and VASODILATORS 12 months pre-RP	1.67	0.00	22.95	1.44	0.00	21.75	1.35	0.00	19.76
Number of rxs of NTG SUBLINGUAL drugs 12 months pre-RP	0.24	0.00	0.79	0.23	0.00	0.85	0.27	0.00	1.08
Number of rxs of VASCULAR DISEASE drugs 12 months pre-RP	0.37	0.00	1.50	0.39	0.00	1.76	0.44	0.00	2.15
Number of rxs of EPILEPSY drugs 12 months pre-RP	0.11	0.00	0.82	0.14	0.00	1.17	0.11	0.00	0.84
Number of rxs of RHEUMATIC DISEASE drugs 12 months pre-RP	0.20	0.00	0.96	0.20	0.00	0.93	0.20	0.00	1.05
Number of rxs of HYPERCHOLESTEROLEMIA drugs 12 months pre-RP	0.57	0.00	1.53	0.49	0.00	1.64	0.49	0.00	1.41
Number of rxs of CANCER drugs 12 months pre-RP	0.03	0.00	0.39	0.06	0.00	0.78	0.02	0.00	0.32
Number of rxs of PARKINSONS DISEASE drugs 12 months pre-RP	0.04	0.00	0.64	0.04	0.00	0.53	0.09	0.00	1.12
Number of rxs of DIABETES drugs 12 months pre-RP	1.01	0.00	3.02	0.57	0.00	2.67	0.75	0.00	2.47
Number of rxs of GLAUCOMA drugs 12 months pre-RP	0.34	0.00	1.66	0.42	0.00	2.13	0.41	0.00	1.90
Number of rxs of CYSTIC FIBROSIS drugs 12 months pre-RP	0.01	0.00	0.25	0.01	0.00	0.25	0.00	0.00	0.14
Number of rxs of RESTRICTED H2RA drugs 12 months pre-RP	0.21	0.00	1.01	0.24	0.00	1.26	0.18	0.00	0.93
Number of rxs of UNRESTRICTED GI PROTECTIVE drugs 12 months pre-RP	0.69	0.00	1.81	0.72	0.00	2.17	0.68	0.00	2.01
Number of rxs of RESPIRATORY drugs 12 months pre-RP	0.80	0.00	3.13	0.51	0.00	2.58	0.65	0.00	2.74
Number of rxs of THYROID drugs 12 months pre-RP	0.51	0.00	1.59	0.49	0.00	1.66	0.44	0.00	1.46
Number of rxs of GOUT drugs 12 months pre-RP	0.19	0.00	0.84	0.19	0.00	1.04	0.20	0.00	0.88
Number of rxs of CROHN'S DISEASE drugs 12 months pre-RP	0.02	0.00	0.47	0.03	0.00	0.63	0.01	0.00	0.12
Number of rxs of RESTRICTED NSAID drugs 12 months pre-RP	0.31	0.00	1.12	0.34	0.00	1.32	0.31	0.00	1.15
Number of rxs of UNRESTRICTED NSAID drugs 12 months pre-RP	0.50	0.00	1.48	0.64	0.00	2.01	0.60	0.00	1.62
Number of rxs of PAIN drugs 12 months pre-RP	0.65	0.00	2.48	0.72	0.00	2.56	0.76	0.00	2.53
Number of rxs of ANTI-DEPRESSANT drugs 12 months pre-RP	0.45	0.00	1.81	0.59	0.00	2.40	0.56	0.00	2.37
Number of rxs of ANTI-PSYCHOSIS drugs 12 months pre-RP	0.08	0.00	0.80	0.12	0.00	1.07	0.20	0.00	1.67
Number of rxs of BIPOLAR DISORDER drugs 12 months pre-RP	0.01	0.00	0.26	0.02	0.00	0.36	0.03	0.00	0.52
Number of rxs of ANTI-ANXIETY drugs 12 months pre-RP	1.18	0.00	3.10	1.38	0.00	3.56	1.25	0.00	3.13
Number of rxs of OTHER drugs 12 months pre-RP	4.81	3.00	6.44	4.77	3.00	6.92	5.06	3.00	7.79

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